UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

VISION BIOSYSTEMS (USA) TRADING INC., Plaintiff, v. VENTANA MEDICAL SYSTEMS, INC., Defendant.	C.A. No. 03-CV-10391-GAO
VENTANA MEDICAL SYSTEMS, INC., Plaintiff, v. VISION BIOSYSTEMS INC., Defendant.	C.A. No. 05-CV-10614-GAO

FIRST DECLARATION OF DOUGLAS E. RINGEL IN SUPPORT OF VISION'S MOTION FOR LEAVE TO SERVE THE ATTACHED EXPERT REPORT FROM DR. BALIS ON THE ISSUE OF OBVIOUSNESS

I, Douglas E. Ringel, declare as follows:

1. I am a member of the law firm of Kenyon & Kenyon LLP, counsel to Vision Biosystems, Inc. ("Vision") in this action. I make this declaration in support of *Vision's Motion For Leave To Serve The Attached Expert Report From Dr. Balis On The Issue Of Obviousness*. The following matters are true of my own personal knowledge.

2. I spoke to Nicole W. Stafford, counsel for Ventana Medical Systems, Inc. ("Ventana"), in an attempt to narrow the areas of disagreement relating to the subject matter of Vision's motion on several occasions.[1] We exchanged several letters following those conversations as well.[2]

3. Our conversations have narrowed the issues of disagreement. On May 1, 2007, Ms. Stafford wrote to me with Ventana's agreement to the parties' exchanging new expert reports on obviousness to take into account any changes in the law as set forth in the Supreme Court's *KSR* decision.[3] However, Ventana's agreement only extended to reports from Ventana's engineering and pathologist experts and Vision's engineering expert—not to Vision's pathologist expert.

4. Attached as **Exhibit A** hereto is a true and correct copy of the slip opinion in *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. __ (2007).

5. Attached as **Exhibit B** hereto is a true and correct copy of a Washington Post article entitled *Rulings Weaken Patents' Power*, dated May 1, 2007.

6. Attached as **Exhibit C** hereto is a true and correct copy of the *Expert Report of Doug Koebler Regarding U.S. Patent No. 6,352,861*, dated April 8, 2004.

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1 I spoke to Ms. Stafford on at least the following dates: April 10, 23 & 30, and May 1, 2007.

2 I wrote to Ms. Stafford on the following dates: April 12, 16, 20 & 30, and May 3, 2007.

3 *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. __ (2007).

7. Attached as **Exhibit D** hereto is a true and correct copy of the *Expert Report of Andre Sharon, Ph.D.*, dated June 8, 2004.

8. Attached as **Exhibit E** hereto is a true and correct copy of the *Expert Report of David Hicks, M.D.*, dated June 8, 2004.

9. Attached as **Exhibit F** hereto is a true and correct copy of the *Supplemental Expert Report of Doug Koebler Regarding U.S. Patent No. 6,352,861*, dated February 18, 2005.

10. Attached as **Exhibit G** hereto is a true and correct copy of the *Second Expert Report of David G. Hicks, M.D.*, dated March 11, 2005.

11. Attached as **Exhibit H** hereto is a true and correct copy of a letter from Elizabeth Leff to Nicole Stafford, dated September 12, 2005.

12. Attached as **Exhibit I** hereto is a true and correct copy of a letter from me to Nicole Stafford, dated April 12, 2007.

13. Attached as **Exhibit J** hereto is a true and correct copy of a letter from me to Nicole Stafford, dated April 16, 2007.

14. Attached as **Exhibit K** hereto is a true and correct copy of a letter from Nicole Stafford to me, dated April 13, 2007.

15. Attached as **Exhibit L** hereto is a true and correct copy of a letter from me to Nicole Stafford, dated May 3, 2007.

16. Attached as **Exhibit M** hereto is a true and correct copy of a letter from Nicole Stafford to me, dated May 1, 2007.

17. Attached as **Exhibit N** hereto is a true and correct copy of an article written by Michael Barclay, a partner in the law firm of Wilson Sonsini Goodrich & Rosati, entitled *Some*

Thoughts About KSR v. Teleflex: The "Marketplace" Test for Obviousness, downloaded from www.scotusblog.com on April 30, 2007.

18. Attached as **Exhibit O** hereto is a true and correct copy of a letter from Pat Skinner to me, dated April 30, 2007.

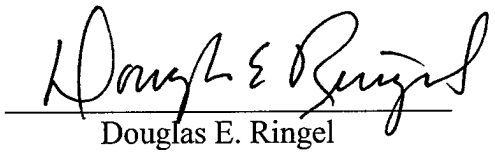
19. Attached as **Exhibit P** hereto is a true and correct copy of U.S. Patent No. 5,122,342 issued to McCulloch.

20. Attached as **Exhibit Q** hereto is a true and correct copy of a letter from Sarah Zimmerman to Elizabeth Leff, dated January 14, 2005.

21. Attached as **Exhibit R** hereto is a true and correct copy of a letter from Judy Day to Elizabeth Leff, dated January 10, 2005.

22. Attached as **Exhibit S** hereto is a true and correct copy of a letter from Sarah Zimmerman to Elizabeth Leff, dated September 21, 2005.

I declare under penalty of perjury that the foregoing is true and correct. Executed on May 7, 2007, in Washington, DC.



Douglas E. Ringel

EXHIBIT A

Syllabus

NOTE: Where it is feasible, a syllabus (headnote) will be released, as is being done in connection with this case, at the time the opinion is issued. The syllabus constitutes no part of the opinion of the Court but has been prepared by the Reporter of Decisions for the convenience of the reader. See *United States* v. *Detroit Timber & Lumber Co.,* 200 U. S. 321, 337.

SUPREME COURT OF THE UNITED STATES

Syllabus

KSR INTERNATIONAL CO. *v.* TELEFLEX INC. ET AL.

CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

No. 04–1350. Argued November 28, 2006—Decided April 30, 2007

To control a conventional automobile's speed, the driver depresses or releases the gas pedal, which interacts with the throttle via a cable or other mechanical link. Because the pedal's position in the footwell normally cannot be adjusted, a driver wishing to be closer or farther from it must either reposition himself in the seat or move the seat, both of which can be imperfect solutions for smaller drivers in cars with deep footwells. This prompted inventors to design and patent pedals that could be adjusted to change their locations. The Asano patent reveals a support structure whereby, when the pedal location is adjusted, one of the pedal's pivot points stays fixed. Asano is also designed so that the force necessary to depress the pedal is the same regardless of location adjustments. The Redding patent reveals a different, sliding mechanism where both the pedal and the pivot point are adjusted.

In newer cars, computer-controlled throttles do not operate through force transferred from the pedal by a mechanical link, but open and close valves in response to electronic signals. For the computer to know what is happening with the pedal, an electronic sensor must translate the mechanical operation into digital data. Inventors had obtained a number of patents for such sensors. The so-called '936 patent taught that it was preferable to detect the pedal's position in the pedal mechanism, not in the engine, so the patent disclosed a pedal with an electronic sensor on a pivot point in the pedal assembly. The Smith patent taught that to prevent the wires connecting the sensor to the computer from chafing and wearing out, the sensor should be put on a fixed part of the pedal assembly rather than in or on the pedal's footpad. Inventors had also patented self-contained modular sensors, which can be taken off the shelf and attached to any

mechanical pedal to allow it to function with a computer-controlled throttle. The '068 patent disclosed one such sensor. Chevrolet also manufactured trucks using modular sensors attached to the pedal support bracket, adjacent to the pedal and engaged with the pivot shaft about which the pedal rotates. Other patents disclose electronic sensors attached to adjustable pedal assemblies. For example, the Rixon patent locates the sensor in the pedal footpad, but is known for wire chafing.

After petitioner KSR developed an adjustable pedal system for cars with cable-actuated throttles and obtained its '976 patent for the design, General Motors Corporation (GMC) chose KSR to supply adjustable pedal systems for trucks using computer-controlled throttles. To make the '976 pedal compatible with the trucks, KSR added a modular sensor to its design. Respondents (Teleflex) hold the exclusive license for the Engelgau patent, claim 4 of which discloses a position-adjustable pedal assembly with an electronic pedal position sensor attached a fixed pivot point. Despite having denied a similar, broader claim, the U. S. Patent and Trademark Office (PTO) had allowed claim 4 because it included the limitation of a fixed pivot position, which distinguished the design from Redding's. Asano was neither included among the Engelgau patent's prior art references nor mentioned in the patent's prosecution, and the PTO did not have before it an adjustable pedal with a fixed pivot point. After learning of KSR's design for GMC, Teleflex sued for infringement, asserting that KSR's pedal system infringed the Engelgau patent's claim 4. KSR countered that claim 4 was invalid under §103 of the Patent Act, which forbids issuance of a patent when "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art."

Graham v. *John Deere Co. of Kansas City*, 383 U. S. 1, 17–18, set out an objective analysis for applying §103: "[T]he scope and content of the prior art are . . . determined; differences between the prior art and the claims at issue are . . . ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." While the sequence of these questions might be reordered in any particular case, the factors define the controlling inquiry. However, seeking to resolve the obviousness question with more uniformity and consistency, the Federal Circuit has employed a "teaching, suggestion, or motivation" (TSM) test, under which a pat-

ent claim is only proved obvious if the prior art, the problem's nature, or the knowledge of a person having ordinary skill in the art reveals some motivation or suggestion to combine the prior art teachings.

The District Court granted KSR summary judgment. After reviewing pedal design history, the Engelgau patent's scope, and the relevant prior art, the court considered claim 4's validity, applying *Graham*'s framework to determine whether under summary-judgment standards KSR had demonstrated that claim 4 was obvious. The court found "little difference" between the prior art's teachings and claim 4: Asano taught everything contained in the claim except using a sensor to detect the pedal's position and transmit it to a computer controlling the throttle. That additional aspect was revealed in, *e.g.,* the '068 patent and Chevrolet's sensors. The court then held that KSR satisfied the TSM test, reasoning (1) the state of the industry would lead inevitably to combinations of electronic sensors and adjustable pedals, (2) Rixon provided the basis for these developments, and (3) Smith taught a solution to Rixon's chafing problems by positioning the sensor on the pedal's fixed structure, which could lead to the combination of a pedal like Asano with a pedal position sensor.

Reversing, the Federal Circuit ruled the District Court had not applied the TSM test strictly enough, having failed to make findings as to the specific understanding or principle within a skilled artisan's knowledge that would have motivated one with no knowledge of the invention to attach an electronic control to the Asano assembly's support bracket. The Court of Appeals held that the District Court's recourse to the nature of the problem to be solved was insufficient because, unless the prior art references addressed the precise problem that the patentee was trying to solve, the problem would not motivate an inventor to look at those references. The appeals court found that the Asano pedal was designed to ensure that the force required to depress the pedal is the same no matter how the pedal is adjusted, whereas Engelgau sought to provide a simpler, smaller, cheaper adjustable electronic pedal. The Rixon pedal, said the court, suffered from chafing but was not designed to solve that problem and taught nothing helpful to Engelgau's purpose. Smith, in turn, did not relate to adjustable pedals and did not necessarily go to the issue of motivation to attach the electronic control on the pedal assembly's support bracket. So interpreted, the court held, the patents would not have led a person of ordinary skill to put a sensor on an Asano-like pedal. That it might have been obvious to try that combination was likewise irrelevant. Finally, the court held that genuine issues of material fact precluded summary judgment.

Held: The Federal Circuit addressed the obviousness question in a narrow, rigid manner that is inconsistent with §103 and this Court's

precedents. KSR provided convincing evidence that mounting an available sensor on a fixed pivot point of the Asano pedal was a design step well within the grasp of a person of ordinary skill in the relevant art and that the benefit of doing so would be obvious. Its arguments, and the record, demonstrate that the Engelgau patent's claim 4 is obvious. Pp. 11–24.

1. *Graham* provided an expansive and flexible approach to the obviousness question that is inconsistent with the way the Federal Circuit applied its TSM test here. Neither §103's enactment nor *Graham*'s analysis disturbed the Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art. See *Great Atlantic & Pacific Tea Co.* v. *Supermarket Equipment Corp.*, 340 U. S. 147, 152. Such a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results. See, *e.g., United States* v. *Adams*, 383 U. S. 39, 50–52. When a work is available in one field, design incentives and other market forces can prompt variations of it, either in the same field or in another. If a person of ordinary skill in the art can implement a predictable variation, and would see the benefit of doing so, §103 likely bars its patentability. Moreover, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill. A court must ask whether the improvement is more than the predictable use of prior-art elements according to their established functions. Following these principles may be difficult if the claimed subject matter involves more than the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement. To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences and creative steps a person of ordinary skill in the art would employ. Pp. 11–14.

(b) The TSM test captures a helpful insight: A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art. Although common sense directs caution as to a patent application claiming as

innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the art to combine the elements as the new invention does. Inventions usually rely upon building blocks long since uncovered, and claimed discoveries almost necessarily will be combinations of what, in some sense, is already known. Helpful insights, however, need not become rigid and mandatory formulas. If it is so applied, the TSM test is incompatible with this Court's precedents. The diversity of inventive pursuits and of modern technology counsels against confining the obviousness analysis by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasizing the importance of published articles and the explicit content of issued patents. In many fields there may be little discussion of obvious techniques or combinations, and market demand, rather than scientific literature, may often drive design trends. Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, for patents combining previously known elements, deprive prior inventions of their value or utility. Since the TSM test was devised, the Federal Circuit doubtless has applied it in accord with these principles in many cases. There is no necessary inconsistency between the test and the *Graham* analysis. But a court errs where, as here, it transforms general principle into a rigid rule limiting the obviousness inquiry. Pp. 14–15.

(c) The flaws in the Federal Circuit's analysis relate mostly to its narrow conception of the obviousness inquiry consequent in its application of the TSM test. The Circuit first erred in holding that courts and patent examiners should look only to the problem the patentee was trying to solve. Under the correct analysis, any need or problem known in the field and addressed by the patent can provide a reason for combining the elements in the manner claimed. Second, the appeals court erred in assuming that a person of ordinary skill in the art attempting to solve a problem will be led only to those prior art elements designed to solve the same problem. The court wrongly concluded that because Asano's primary purpose was solving the constant ratio problem, an inventor considering how to put a sensor on an adjustable pedal would have no reason to consider putting it on the Asano pedal. It is common sense that familiar items may have obvious uses beyond their primary purposes, and a person of ordinary skill often will be able to fit the teachings of multiple patents together like pieces of a puzzle. Regardless of Asano's primary purpose, it provided an obvious example of an adjustable pedal with a fixed pivot point, and the prior art was replete with patents indicating that such a point was an ideal mount for a sensor. Third, the

court erred in concluding that a patent claim cannot be proved obvious merely by showing that the combination of elements was obvious to try. When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. Finally, the court drew the wrong conclusion from the risk of courts and patent examiners falling prey to hindsight bias. Rigid preventative rules that deny recourse to common sense are neither necessary under, nor consistent with, this Court's case law. Pp. 15–18.

2. Application of the foregoing standards demonstrates that claim 4 is obvious. Pp. 18–23.

(a) The Court rejects Teleflex's argument that the Asano pivot mechanism's design prevents its combination with a sensor in the manner claim 4 describes. This argument was not raised before the District Court, and it is unclear whether it was raised before the Federal Circuit. Given the significance of the District Court's finding that combining Asano with a pivot-mounted pedal position sensor fell within claim 4's scope, it is apparent that Teleflex would have made clearer challenges if it intended to preserve this claim. Its failure to clearly raise the argument, and the appeals court's silence on the issue, lead this Court to accept the District Court's conclusion. Pp. 18–20.

(b) The District Court correctly concluded that when Engelgau designed the claim 4 subject matter, it was obvious to a person of ordinary skill in the art to combine Asano with a pivot-mounted pedal position sensor. There then was a marketplace creating a strong incentive to convert mechanical pedals to electronic pedals, and the prior art taught a number of methods for doing so. The Federal Circuit considered the issue too narrowly by, in effect, asking whether a pedal designer writing on a blank slate would have chosen both Asano and a modular sensor similar to the ones used in the Chevrolet trucks and disclosed in the '068 patent. The proper question was whether a pedal designer of ordinary skill in the art, facing the wide range of needs created by developments in the field, would have seen an obvious benefit to upgrading Asano with a sensor. For such a designer starting with Asano, the question was where to attach the sensor. The '936 patent taught the utility of putting the sensor on the pedal device. Smith, in turn, explained not to put the sensor on the pedal footpad, but instead on the structure. And from Rixon's known wire-chafing problems, and Smith's teaching that the pedal assemblies must not precipitate any motion in the connecting wires,

the designer would know to place the sensor on a nonmoving part of the pedal structure. The most obvious such point is a pivot point. The designer, accordingly, would follow Smith in mounting the sensor there. Just as it was possible to begin with the objective to upgrade Asano to work with a computer-controlled throttle, so too was it possible to take an adjustable electronic pedal like Rixon and seek an improvement that would avoid the wire-chafing problem. Teleflex has not shown anything in the prior art that taught away from the use of Asano, nor any secondary factors to dislodge the determination that claim 4 is obvious. Pp. 20–23.

3. The Court disagrees with the Federal Circuit's holding that genuine issues of material fact precluded summary judgment. The ultimate judgment of obviousness is a legal determination. *Graham*, 383 U. S., at 17. Where, as here, the prior art's content, the patent claim's scope, and the level of ordinary skill in the art are not in material dispute and the claim's obviousness is apparent, summary judgment is appropriate. P. 23.

119 Fed. Appx. 282, reversed and remanded.

KENNEDY, J., delivered the opinion for a unanimous Court.

SUPREME COURT OF THE UNITED STATES

No. 04–1350

KSR INTERNATIONAL CO., PETITIONER *v.*
TELEFLEX INC. ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

[April 30, 2007]

JUSTICE KENNEDY delivered the opinion of the Court.

Teleflex Incorporated and its subsidiary Technology Holding Company—both referred to here as Teleflex—sued KSR International Company for patent infringement. The patent at issue, United States Patent No. 6,237,565 B1, is entitled "Adjustable Pedal Assembly With Electronic Throttle Control." Supplemental App. 1. The patentee is Steven J. Engelgau, and the patent is referred to as "the Engelgau patent." Teleflex holds the exclusive license to the patent.

Claim 4 of the Engelgau patent describes a mechanism for combining an electronic sensor with an adjustable automobile pedal so the pedal's position can be transmitted to a computer that controls the throttle in the vehicle's engine. When Teleflex accused KSR of infringing the Engelgau patent by adding an electronic sensor to one of KSR's previously designed pedals, KSR countered that claim 4 was invalid under the Patent Act, 35 U. S. C. §103, because its subject matter was obvious.

Section 103 forbids issuance of a patent when "the differences between the subject matter sought to be pat-

ented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains."

In *Graham* v. *John Deere Co. of Kansas City*, 383 U. S. 1 (1966), the Court set out a framework for applying the statutory language of §103, language itself based on the logic of the earlier decision in *Hotchkiss* v. *Greenwood*, 11 How. 248 (1851), and its progeny. See 383 U. S., at 15–17. The analysis is objective:

> "Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *Id.*, at 17–18.

While the sequence of these questions might be reordered in any particular case, the factors continue to define the inquiry that controls. If a court, or patent examiner, conducts this analysis and concludes the claimed subject matter was obvious, the claim is invalid under §103.

Seeking to resolve the question of obviousness with more uniformity and consistency, the Court of Appeals for the Federal Circuit has employed an approach referred to by the parties as the "teaching, suggestion, or motivation" test (TSM test), under which a patent claim is only proved obvious if "some motivation or suggestion to combine the prior art teachings" can be found in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art. See, *e.g., Al-Site Corp.* v. *VSI*

Int'l, Inc., 174 F. 3d 1308, 1323–1324 (CA Fed. 1999). KSR challenges that test, or at least its application in this case. See 119 Fed. Appx. 282, 286–290 (CA Fed. 2005). Because the Court of Appeals addressed the question of obviousness in a manner contrary to §103 and our precedents, we granted certiorari, 547 U. S ___ (2006). We now reverse.

I

A

In car engines without computer-controlled throttles, the accelerator pedal interacts with the throttle via cable or other mechanical link. The pedal arm acts as a lever rotating around a pivot point. In a cable-actuated throttle control the rotation caused by pushing down the pedal pulls a cable, which in turn pulls open valves in the carburetor or fuel injection unit. The wider the valves open, the more fuel and air are released, causing combustion to increase and the car to accelerate. When the driver takes his foot off the pedal, the opposite occurs as the cable is released and the valves slide closed.

In the 1990's it became more common to install computers in cars to control engine operation. Computer-controlled throttles open and close valves in response to electronic signals, not through force transferred from the pedal by a mechanical link. Constant, delicate adjustments of air and fuel mixture are possible. The computer's rapid processing of factors beyond the pedal's position improves fuel efficiency and engine performance.

For a computer-controlled throttle to respond to a driver's operation of the car, the computer must know what is happening with the pedal. A cable or mechanical link does not suffice for this purpose; at some point, an electronic sensor is necessary to translate the mechanical operation into digital data the computer can understand.

Before discussing sensors further we turn to the me-

chanical design of the pedal itself. In the traditional design a pedal can be pushed down or released but cannot have its position in the footwell adjusted by sliding the pedal forward or back. As a result, a driver who wishes to be closer or farther from the pedal must either reposition himself in the driver's seat or move the seat in some way. In cars with deep footwells these are imperfect solutions for drivers of smaller stature. To solve the problem, inventors, beginning in the 1970's, designed pedals that could be adjusted to change their location in the footwell. Important for this case are two adjustable pedals disclosed in U. S. Patent Nos. 5,010,782 (filed July 28, 1989) (Asano) and 5,460,061 (filed Sept. 17, 1993) (Redding). The Asano patent reveals a support structure that houses the pedal so that even when the pedal location is adjusted relative to the driver, one of the pedal's pivot points stays fixed. The pedal is also designed so that the force necessary to push the pedal down is the same regardless of adjustments to its location. The Redding patent reveals a different, sliding mechanism where both the pedal and the pivot point are adjusted.

We return to sensors. Well before Engelgau applied for his challenged patent, some inventors had obtained patents involving electronic pedal sensors for computer-controlled throttles. These inventions, such as the device disclosed in U. S. Patent No. 5,241,936 (filed Sept. 9, 1991) ('936), taught that it was preferable to detect the pedal's position in the pedal assembly, not in the engine. The '936 patent disclosed a pedal with an electronic sensor on a pivot point in the pedal assembly. U. S. Patent No. 5,063,811 (filed July 9, 1990) (Smith) taught that to prevent the wires connecting the sensor to the computer from chafing and wearing out, and to avoid grime and damage from the driver's foot, the sensor should be put on a fixed part of the pedal assembly rather than in or on the pedal's footpad.

In addition to patents for pedals with integrated sensors inventors obtained patents for self-contained modular sensors. A modular sensor is designed independently of a given pedal so that it can be taken off the shelf and attached to mechanical pedals of various sorts, enabling the pedals to be used in automobiles with computer-controlled throttles. One such sensor was disclosed in U. S. Patent No. 5,385,068 (filed Dec. 18, 1992) ('068). In 1994, Chevrolet manufactured a line of trucks using modular sensors "attached to the pedal support bracket, adjacent to the pedal and engaged with the pivot shaft about which the pedal rotates in operation." 298 F. Supp. 2d 581, 589 (ED Mich. 2003).

The prior art contained patents involving the placement of sensors on adjustable pedals as well. For example, U. S. Patent No. 5,819,593 (filed Aug. 17, 1995) (Rixon) discloses an adjustable pedal assembly with an electronic sensor for detecting the pedal's position. In the Rixon pedal the sensor is located in the pedal footpad. The Rixon pedal was known to suffer from wire chafing when the pedal was depressed and released.

This short account of pedal and sensor technology leads to the instant case.

B

KSR, a Canadian company, manufactures and supplies auto parts, including pedal systems. Ford Motor Company hired KSR in 1998 to supply an adjustable pedal system for various lines of automobiles with cable-actuated throttle controls. KSR developed an adjustable mechanical pedal for Ford and obtained U. S. Patent No. 6,151,976 (filed July 16, 1999) ('976) for the design. In 2000, KSR was chosen by General Motors Corporation (GMC or GM) to supply adjustable pedal systems for Chevrolet and GMC light trucks that used engines with computer-controlled throttles. To make the '976 pedal compatible with the

trucks, KSR merely took that design and added a modular sensor.

Teleflex is a rival to KSR in the design and manufacture of adjustable pedals. As noted, it is the exclusive licensee of the Engelgau patent. Engelgau filed the patent application on August 22, 2000 as a continuation of a previous application for U. S. Patent No. 6,109,241, which was filed on January 26, 1999. He has sworn he invented the patent's subject matter on February 14, 1998. The Engelgau patent discloses an adjustable electronic pedal described in the specification as a "simplified vehicle control pedal assembly that is less expensive, and which uses fewer parts and is easier to package within the vehicle." Engelgau, col. 2, lines 2–5, Supplemental App. 6. Claim 4 of the patent, at issue here, describes:

> "A vehicle control pedal apparatus comprising:
>
> a support adapted to be mounted to a vehicle structure;
>
> an adjustable pedal assembly having a pedal arm moveable in for[e] and aft directions with respect to said support;
>
> a pivot for pivotally supporting said adjustable pedal assembly with respect to said support and defining a pivot axis; and
>
> an electronic control attached to said support for controlling a vehicle system;
>
> said apparatus characterized by said electronic control being responsive to said pivot for providing a signal that corresponds to pedal arm position as said pedal arm pivots about said pivot axis between rest and applied positions wherein the position of said pivot remains constant while said pedal arm moves in fore and aft directions with respect to said pivot." *Id.,* col.

> 6, lines 17–36, Supplemental App. 8 (diagram numbers omitted).

We agree with the District Court that the claim discloses "a position-adjustable pedal assembly with an electronic pedal position sensor attached to the support member of the pedal assembly. Attaching the sensor to the support member allows the sensor to remain in a fixed position while the driver adjusts the pedal." 298 F. Supp. 2d, at 586–587.

Before issuing the Engelgau patent the U. S. Patent and Trademark Office (PTO) rejected one of the patent claims that was similar to, but broader than, the present claim 4. The claim did not include the requirement that the sensor be placed on a fixed pivot point. The PTO concluded the claim was an obvious combination of the prior art disclosed in Redding and Smith, explaining:

> "'Since the prior ar[t] references are from the field of endeavor, the purpose disclosed . . . would have been recognized in the pertinent art of Redding. Therefore it would have been obvious . . . to provide the device of Redding with the . . . means attached to a support member as taught by Smith.'" *Id.*, at 595.

In other words Redding provided an example of an adjustable pedal and Smith explained how to mount a sensor on a pedal's support structure, and the rejected patent claim merely put these two teachings together.

Although the broader claim was rejected, claim 4 was later allowed because it included the limitation of a fixed pivot point, which distinguished the design from Redding's. *Ibid*. Engelgau had not included Asano among the prior art references, and Asano was not mentioned in the patent's prosecution. Thus, the PTO did not have before it an adjustable pedal with a fixed pivot point. The patent issued on May 29, 2001 and was assigned to Teleflex.

Upon learning of KSR's design for GM, Teleflex sent a

warning letter informing KSR that its proposal would violate the Engelgau patent. "'Teleflex believes that any supplier of a product that combines an adjustable pedal with an electronic throttle control necessarily employs technology covered by one or more'" of Teleflex's patents. *Id.*, at 585. KSR refused to enter a royalty arrangement with Teleflex; so Teleflex sued for infringement, asserting KSR's pedal infringed the Engelgau patent and two other patents. *Ibid.* Teleflex later abandoned its claims regarding the other patents and dedicated the patents to the public. The remaining contention was that KSR's pedal system for GM infringed claim 4 of the Engelgau patent. Teleflex has not argued that the other three claims of the patent are infringed by KSR's pedal, nor has Teleflex argued that the mechanical adjustable pedal designed by KSR for Ford infringed any of its patents.

C

The District Court granted summary judgment in KSR's favor. After reviewing the pertinent history of pedal design, the scope of the Engelgau patent, and the relevant prior art, the court considered the validity of the contested claim. By direction of 35 U. S. C. §282, an issued patent is presumed valid. The District Court applied *Graham*'s framework to determine whether under summary-judgment standards KSR had overcome the presumption and demonstrated that claim 4 was obvious in light of the prior art in existence when the claimed subject matter was invented. See §102(a).

The District Court determined, in light of the expert testimony and the parties' stipulations, that the level of ordinary skill in pedal design was "'an undergraduate degree in mechanical engineering (or an equivalent amount of industry experience) [and] familiarity with pedal control systems for vehicles.'" 298 F. Supp. 2d, at 590. The court then set forth the relevant prior art, in-

cluding the patents and pedal designs described above.

Following *Graham*'s direction, the court compared the teachings of the prior art to the claims of Engelgau. It found "little difference." 298 F. Supp. 2d, at 590. Asano taught everything contained in claim 4 except the use of a sensor to detect the pedal's position and transmit it to the computer controlling the throttle. That additional aspect was revealed in sources such as the '068 patent and the sensors used by Chevrolet.

Under the controlling cases from the Court of Appeals for the Federal Circuit, however, the District Court was not permitted to stop there. The court was required also to apply the TSM test. The District Court held KSR had satisfied the test. It reasoned (1) the state of the industry would lead inevitably to combinations of electronic sensors and adjustable pedals, (2) Rixon provided the basis for these developments, and (3) Smith taught a solution to the wire chafing problems in Rixon, namely locating the sensor on the fixed structure of the pedal. This could lead to the combination of Asano, or a pedal like it, with a pedal position sensor.

The conclusion that the Engelgau design was obvious was supported, in the District Court's view, by the PTO's rejection of the broader version of claim 4. Had Engelgau included Asano in his patent application, it reasoned, the PTO would have found claim 4 to be an obvious combination of Asano and Smith, as it had found the broader version an obvious combination of Redding and Smith. As a final matter, the District Court held that the secondary factor of Teleflex's commercial success with pedals based on Engelgau's design did not alter its conclusion. The District Court granted summary judgment for KSR.

With principal reliance on the TSM test, the Court of Appeals reversed. It ruled the District Court had not been strict enough in applying the test, having failed to make "'finding[s] as to the specific understanding or principle

within the knowledge of a skilled artisan that would have motivated one with no knowledge of [the] invention' . . . to attach an electronic control to the support bracket of the Asano assembly." 119 Fed. Appx., at 288 (brackets in original) (quoting *In re Kotzab*, 217 F. 3d 1365, 1371 (CA Fed. 2000)). The Court of Appeals held that the District Court was incorrect that the nature of the problem to be solved satisfied this requirement because unless the "prior art references address[ed] the precise problem that the patentee was trying to solve," the problem would not motivate an inventor to look at those references. 119 Fed. Appx., at 288.

Here, the Court of Appeals found, the Asano pedal was designed to solve the "'constant ratio problem'"—that is, to ensure that the force required to depress the pedal is the same no matter how the pedal is adjusted—whereas Engelgau sought to provide a simpler, smaller, cheaper adjustable electronic pedal. *Ibid.* As for Rixon, the court explained, that pedal suffered from the problem of wire chafing but was not designed to solve it. In the court's view Rixon did not teach anything helpful to Engelgau's purpose. Smith, in turn, did not relate to adjustable pedals and did not "necessarily go to the issue of motivation to attach the electronic control on the support bracket of the pedal assembly." *Ibid.* When the patents were interpreted in this way, the Court of Appeals held, they would not have led a person of ordinary skill to put a sensor on the sort of pedal described in Asano.

That it might have been obvious to try the combination of Asano and a sensor was likewise irrelevant, in the court's view, because "'"[o]bvious to try" has long been held not to constitute obviousness.'" *Id.*, at 289 (quoting *In re Deuel*, 51 F. 3d 1552, 1559 (CA Fed. 1995)).

The Court of Appeals also faulted the District Court's consideration of the PTO's rejection of the broader version of claim 4. The District Court's role, the Court of Appeals

explained, was not to speculate regarding what the PTO might have done had the Engelgau patent mentioned Asano. Rather, the court held, the District Court was obliged first to presume that the issued patent was valid and then to render its own independent judgment of obviousness based on a review of the prior art. The fact that the PTO had rejected the broader version of claim 4, the Court of Appeals said, had no place in that analysis.

The Court of Appeals further held that genuine issues of material fact precluded summary judgment. Teleflex had proffered statements from one expert that claim 4 "'was a simple, elegant, and novel combination of features,'" 119 Fed. Appx., at 290, compared to Rixon, and from another expert that claim 4 was nonobvious because, unlike in Rixon, the sensor was mounted on the support bracket rather than the pedal itself. This evidence, the court concluded, sufficed to require a trial.

II

A

We begin by rejecting the rigid approach of the Court of Appeals. Throughout this Court's engagement with the question of obviousness, our cases have set forth an expansive and flexible approach inconsistent with the way the Court of Appeals applied its TSM test here. To be sure, *Graham* recognized the need for "uniformity and definiteness." 383 U. S., at 18. Yet the principles laid down in *Graham* reaffirmed the "functional approach" of *Hotchkiss*, 11 How. 248. See 383 U. S., at 12. To this end, *Graham* set forth a broad inquiry and invited courts, where appropriate, to look at any secondary considerations that would prove instructive. *Id.*, at 17.

Neither the enactment of §103 nor the analysis in *Graham* disturbed this Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art. For over a

half century, the Court has held that a "patent for a combination which only unites old elements with no change in their respective functions . . . obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." *Great Atlantic & Pacific Tea Co.* v. *Supermarket Equipment Corp.*, 340 U. S. 147, 152 (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results. Three cases decided after *Graham* illustrate the application of this doctrine.

In *United States* v. *Adams*, 383 U. S. 39, 40 (1966), a companion case to *Graham*, the Court considered the obviousness of a "wet battery" that varied from prior designs in two ways: It contained water, rather than the acids conventionally employed in storage batteries; and its electrodes were magnesium and cuprous chloride, rather than zinc and silver chloride. The Court recognized that when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result. 383 U. S., at 50–51. It nevertheless rejected the Government's claim that Adams's battery was obvious. The Court relied upon the corollary principle that when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious. *Id.*, at 51–52. When Adams designed his battery, the prior art warned that risks were involved in using the types of electrodes he employed. The fact that the elements worked together in an unexpected and fruitful manner supported the conclusion that Adams's design was not obvious to those skilled in the art.

In *Anderson's-Black Rock, Inc.* v. *Pavement Salvage Co.*, 396 U. S. 57 (1969), the Court elaborated on this approach.

The subject matter of the patent before the Court was a device combining two pre-existing elements: a radiant-heat burner and a paving machine. The device, the Court concluded, did not create some new synergy: The radiant-heat burner functioned just as a burner was expected to function; and the paving machine did the same. The two in combination did no more than they would in separate, sequential operation. *Id.*, at 60–62. In those circumstances, "while the combination of old elements performed a useful function, it added nothing to the nature and quality of the radiant-heat burner already patented," and the patent failed under §103. *Id.,* at 62 (footnote omitted).

Finally, in *Sakraida* v. *AG Pro, Inc.*, 425 U. S. 273 (1976), the Court derived from the precedents the conclusion that when a patent "simply arranges old elements with each performing the same function it had been known to perform" and yields no more than one would expect from such an arrangement, the combination is obvious. *Id.*, at 282.

The principles underlying these cases are instructive when the question is whether a patent claiming the combination of elements of prior art is obvious. When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. *Sakraida* and *Anderson's-Black Rock* are illustrative—a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

Following these principles may be more difficult in other

cases than it is here because the claimed subject matter may involve more than the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement. Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit. See *In re Kahn*, 441 F. 3d 977, 988 (CA Fed. 2006) ("[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness"). As our precedents make clear, however, the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.

B

When it first established the requirement of demonstrating a teaching, suggestion, or motivation to combine known elements in order to show that the combination is obvious, the Court of Customs and Patent Appeals captured a helpful insight. See *Application of Bergel,* 292 F. 2d 955, 956–957 (1961). As is clear from cases such as *Adams*, a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established

functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Helpful insights, however, need not become rigid and mandatory formulas; and when it is so applied, the TSM test is incompatible with our precedents. The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents. The diversity of inventive pursuits and of modern technology counsels against limiting the analysis in this way. In many fields it may be that there is little discussion of obvious techniques or combinations, and it often may be the case that market demand, rather than scientific literature, will drive design trends. Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility.

In the years since the Court of Customs and Patent Appeals set forth the essence of the TSM test, the Court of Appeals no doubt has applied the test in accord with these principles in many cases. There is no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis. But when a court transforms the general principle into a rigid rule that limits the obviousness inquiry, as the Court of Appeals did here, it errs.

C

The flaws in the analysis of the Court of Appeals relate

for the most part to the court's narrow conception of the obviousness inquiry reflected in its application of the TSM test. In determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls. What matters is the objective reach of the claim. If the claim extends to what is obvious, it is invalid under §103. One of the ways in which a patent's subject matter can be proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims.

The first error of the Court of Appeals in this case was to foreclose this reasoning by holding that courts and patent examiners should look only to the problem the patentee was trying to solve. 119 Fed. Appx., at 288. The Court of Appeals failed to recognize that the problem motivating the patentee may be only one of many addressed by the patent's subject matter. The question is not whether the combination was obvious to the patentee but whether the combination was obvious to a person with ordinary skill in the art. Under the correct analysis, any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.

The second error of the Court of Appeals lay in its assumption that a person of ordinary skill attempting to solve a problem will be led only to those elements of prior art designed to solve the same problem. *Ibid.* The primary purpose of Asano was solving the constant ratio problem; so, the court concluded, an inventor considering how to put a sensor on an adjustable pedal would have no reason to consider putting it on the Asano pedal. *Ibid.* Common sense teaches, however, that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a

puzzle. Regardless of Asano's primary purpose, the design provided an obvious example of an adjustable pedal with a fixed pivot point; and the prior art was replete with patents indicating that a fixed pivot point was an ideal mount for a sensor. The idea that a designer hoping to make an adjustable electronic pedal would ignore Asano because Asano was designed to solve the constant ratio problem makes little sense. A person of ordinary skill is also a person of ordinary creativity, not an automaton.

The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." *Id.*, at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103.

The Court of Appeals, finally, drew the wrong conclusion from the risk of courts and patent examiners falling prey to hindsight bias. A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning. See *Graham*, 383 U. S., at 36 (warning against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to "'guard against slipping into the use of hindsight'" (quoting *Monroe Auto Equipment Co.* v. *Heckethorn Mfg. & Supply Co.*, 332 F. 2d 406, 412 (CA6 1964))). Rigid preventative rules that deny factfinders recourse to common sense, however, are neither necessary under our case law nor consistent with it.

We note the Court of Appeals has since elaborated a

broader conception of the TSM test than was applied in the instant matter. See, *e.g., DyStar Textilfarben GmbH & Co. Deutschland KG* v. *C. H. Patrick Co.*, 464 F. 3d 1356, 1367 (2006) ("Our suggestion test is in actuality quite flexible and not only permits, but *requires*, consideration of common knowledge and common sense"); *Alza Corp.* v. *Mylan Labs., Inc.*, 464 F. 3d 1286, 1291 (2006) ("There is flexibility in our obviousness jurisprudence because a motivation may be found *implicitly* in the prior art. We do not have a rigid test that requires an actual teaching to combine . . ."). Those decisions, of course, are not now before us and do not correct the errors of law made by the Court of Appeals in this case. The extent to which they may describe an analysis more consistent with our earlier precedents and our decision here is a matter for the Court of Appeals to consider in its future cases. What we hold is that the fundamental misunderstandings identified above led the Court of Appeals in this case to apply a test inconsistent with our patent law decisions.

III

When we apply the standards we have explained to the instant facts, claim 4 must be found obvious. We agree with and adopt the District Court's recitation of the relevant prior art and its determination of the level of ordinary skill in the field. As did the District Court, we see little difference between the teachings of Asano and Smith and the adjustable electronic pedal disclosed in claim 4 of the Engelgau patent. A person having ordinary skill in the art could have combined Asano with a pedal position sensor in a fashion encompassed by claim 4, and would have seen the benefits of doing so.

A

Teleflex argues in passing that the Asano pedal cannot be combined with a sensor in the manner described by

claim 4 because of the design of Asano's pivot mechanisms. See Brief for Respondents 48–49, and n. 17. Therefore, Teleflex reasons, even if adding a sensor to Asano was obvious, that does not establish that claim 4 encompasses obvious subject matter. This argument was not, however, raised before the District Court. There Teleflex was content to assert only that the problem motivating the invention claimed by the Engelgau patent would not lead to the solution of combining of Asano with a sensor. See Teleflex's Response to KSR's Motion for Summary Judgment of Invalidity in No. 02–74586 (ED Mich.), pp. 18–20, App. 144a–146a. It is also unclear whether the current argument was raised before the Court of Appeals, where Teleflex advanced the nonspecific, conclusory contention that combining Asano with a sensor would not satisfy the limitations of claim 4. See Brief for Plaintiffs-Appellants in No. 04–1152 (CA Fed.), pp. 42–44. Teleflex's own expert declarations, moreover, do not support the point Teleflex now raises. See Declaration of Clark J. Radcliffe, Ph.D., Supplemental App. 204–207; Declaration of Timothy L. Andresen, *id.,* at 208–210. The only statement in either declaration that might bear on the argument is found in the Radcliffe declaration:

> "Asano . . . and Rixon . . . are complex mechanical linkage-based devices that are expensive to produce and assemble and difficult to package. It is exactly these difficulties with prior art designs that [Engelgau] resolves. The use of an adjustable pedal with a single pivot reflecting pedal position combined with an electronic control mounted between the support and the adjustment assembly at that pivot was a simple, elegant, and novel combination of features in the Engelgau '565 patent." *Id.,* at 206, ¶16.

Read in the context of the declaration as a whole this is best interpreted to mean that Asano could not be used to

solve "[t]he problem addressed by Engelgau '565[:] to provide a less expensive, more quickly assembled, and smaller package adjustable pedal assembly with electronic control." *Id.*, at 205, ¶10.

The District Court found that combining Asano with a pivot-mounted pedal position sensor fell within the scope of claim 4. 298 F. Supp. 2d, at 592–593. Given the sigificance of that finding to the District Court's judgment, it is apparent that Teleflex would have made clearer challenges to it if it intended to preserve this claim. In light of Teleflex's failure to raise the argument in a clear fashion, and the silence of the Court of Appeals on the issue, we take the District Court's conclusion on the point to be correct.

B

The District Court was correct to conclude that, as of the time Engelgau designed the subject matter in claim 4, it was obvious to a person of ordinary skill to combine Asano with a pivot-mounted pedal position sensor. There then existed a marketplace that created a strong incentive to convert mechanical pedals to electronic pedals, and the prior art taught a number of methods for achieving this advance. The Court of Appeals considered the issue too narrowly by, in effect, asking whether a pedal designer writing on a blank slate would have chosen both Asano and a modular sensor similar to the ones used in the Chevrolet truckline and disclosed in the '068 patent. The District Court employed this narrow inquiry as well, though it reached the correct result nevertheless. The proper question to have asked was whether a pedal designer of ordinary skill, facing the wide range of needs created by developments in the field of endeavor, would have seen a benefit to upgrading Asano with a sensor.

In automotive design, as in many other fields, the interaction of multiple components means that changing one

component often requires the others to be modified as well. Technological developments made it clear that engines using computer-controlled throttles would become standard. As a result, designers might have decided to design new pedals from scratch; but they also would have had reason to make pre-existing pedals work with the new engines. Indeed, upgrading its own pre-existing model led KSR to design the pedal now accused of infringing the Engelgau patent.

For a designer starting with Asano, the question was where to attach the sensor. The consequent legal question, then, is whether a pedal designer of ordinary skill starting with Asano would have found it obvious to put the sensor on a fixed pivot point. The prior art discussed above leads us to the conclusion that attaching the sensor where both KSR and Engelgau put it would have been obvious to a person of ordinary skill.

The '936 patent taught the utility of putting the sensor on the pedal device, not in the engine. Smith, in turn, explained to put the sensor not on the pedal's footpad but instead on its support structure. And from the known wire-chafing problems of Rixon, and Smith's teaching that "the pedal assemblies must not precipitate any motion in the connecting wires," Smith, col. 1, lines 35–37, Supplemental App. 274, the designer would know to place the sensor on a nonmoving part of the pedal structure. The most obvious nonmoving point on the structure from which a sensor can easily detect the pedal's position is a pivot point. The designer, accordingly, would follow Smith in mounting the sensor on a pivot, thereby designing an adjustable electronic pedal covered by claim 4.

Just as it was possible to begin with the objective to upgrade Asano to work with a computer-controlled throttle, so too was it possible to take an adjustable electronic pedal like Rixon and seek an improvement that would avoid the wire-chafing problem. Following similar steps to

those just explained, a designer would learn from Smith to avoid sensor movement and would come, thereby, to Asano because Asano disclosed an adjustable pedal with a fixed pivot.

Teleflex indirectly argues that the prior art taught away from attaching a sensor to Asano because Asano in its view is bulky, complex, and expensive. The only evidence Teleflex marshals in support of this argument, however, is the Radcliffe declaration, which merely indicates that Asano would not have solved Engelgau's goal of making a small, simple, and inexpensive pedal. What the declaration does not indicate is that Asano was somehow so flawed that there was no reason to upgrade it, or pedals like it, to be compatible with modern engines. Indeed, Teleflex's own declarations refute this conclusion. Dr. Radcliffe states that Rixon suffered from the same bulk and complexity as did Asano. See *id.,* at 206. Teleflex's other expert, however, explained that Rixon was itself designed by adding a sensor to a pre-existing mechanical pedal. See *id.,* at 209. If Rixon's base pedal was not too flawed to upgrade, then Dr. Radcliffe's declaration does not show Asano was either. Teleflex may have made a plausible argument that Asano is inefficient as compared to Engelgau's preferred embodiment, but to judge Asano against Engelgau would be to engage in the very hindsight bias Teleflex rightly urges must be avoided. Accordingly, Teleflex has not shown anything in the prior art that taught away from the use of Asano.

Like the District Court, finally, we conclude Teleflex has shown no secondary factors to dislodge the determination that claim 4 is obvious. Proper application of *Graham* and our other precedents to these facts therefore leads to the conclusion that claim 4 encompassed obvious subject matter. As a result, the claim fails to meet the requirement of §103.

We need not reach the question whether the failure to

disclose Asano during the prosecution of Engelgau voids the presumption of validity given to issued patents, for claim 4 is obvious despite the presumption. We nevertheless think it appropriate to note that the rationale underlying the presumption—that the PTO, in its expertise, has approved the claim—seems much diminished here.

IV

A separate ground the Court of Appeals gave for reversing the order for summary judgment was the existence of a dispute over an issue of material fact. We disagree with the Court of Appeals on this point as well. To the extent the court understood the *Graham* approach to exclude the possibility of summary judgment when an expert provides a conclusory affidavit addressing the question of obviousness, it misunderstood the role expert testimony plays in the analysis. In considering summary judgment on that question the district court can and should take into account expert testimony, which may resolve or keep open certain questions of fact. That is not the end of the issue, however. The ultimate judgment of obviousness is a legal determination. *Graham*, 383 U. S., at 17. Where, as here, the content of the prior art, the scope of the patent claim, and the level of ordinary skill in the art are not in material dispute, and the obviousness of the claim is apparent in light of these factors, summary judgment is appropriate. Nothing in the declarations proffered by Teleflex prevented the District Court from reaching the careful conclusions underlying its order for summary judgment in this case.

* * *

We build and create by bringing to the tangible and palpable reality around us new works based on instinct, simple logic, ordinary inferences, extraordinary ideas, and sometimes even genius. These advances, once part of our

shared knowledge, define a new threshold from which innovation starts once more. And as progress beginning from higher levels of achievement is expected in the normal course, the results of ordinary innovation are not the subject of exclusive rights under the patent laws. Were it otherwise patents might stifle, rather than promote, the progress of useful arts. See U. S. Const., Art. I, §8, cl. 8. These premises led to the bar on patents claiming obvious subject matter established in *Hotchkiss* and codified in §103. Application of the bar must not be confined within a test or formulation too constrained to serve its purpose.

KSR provided convincing evidence that mounting a modular sensor on a fixed pivot point of the Asano pedal was a design step well within the grasp of a person of ordinary skill in the relevant art. Its arguments, and the record, demonstrate that claim 4 of the Engelgau patent is obvious. In rejecting the District Court's rulings, the Court of Appeals analyzed the issue in a narrow, rigid manner inconsistent with §103 and our precedents. The judgment of the Court of Appeals is reversed, and the case remanded for further proceedings consistent with this opinion.

It is so ordered.

EXHIBIT B

Rulings Weaken Patents' Power

High Court Decides On Two Key Cases

By Robert Barnes and Alan Sipress
Washington Post Staff Writers
Tuesday, May 1, 2007; D01

The Supreme Court concluded a series of cases yesterday that weaken the protection given to patent holders, making it more difficult to get a patent and easier to challenge existing ones.

Patent experts said one of two cases decided yesterday -- *KSR International v. Teleflex*-- is the court's furthest-reaching ruling in the field for decades. The decision sends a clear message that the U.S. Patent and Trademark Office and lower courts must be more open in considering whether inventions are "obvious," a common ground for denying an application.

"Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility," Justice Anthony M. Kennedy wrote for a unanimous court.

In a separate case, the court ruled yesterday that Microsoft did not violate an AT&T patent when its Windows software was installed on computers manufactured overseas.

"The presumption that United State law governs domestically but does not rule the world applies with particular force in patent law," Justice Ruth Bader Ginsburg wrote in the 7 to 1 decision. Justice John Paul Stevens dissented, and Chief Justice John G. Roberts Jr. recused himself from the case.

Although the cases -- along with the earlier-decided *MedImmune v. Genentech*-- concerned different aspects of the law, experts said the cases collectively show a Supreme Court united in its belief that patent holders have received too much protection in the past.

"We now have a string of decisions that say the Supreme Court thinks we have too many patents and it's too hard to invalidate them," said Thomas C. Goldstein, a lawyer for Teleflex. "It's hard to miss that message."

The KSR and MedImmune cases together mean much less certainty for holders of thousands of existing patents, said John R. Thomas, a Georgetown University law professor who specializes in intellectual property. "The bottom-line effect is that interested parties have a greater ability to challenge patents and a greater possibility of prevailing."

The disputed patent in the KSR case was held by Teleflex and involved an adjustable gas pedal that combined two established elements, the pedal and an electronic sensor. KSR, a Canadian company, challenged the patent, and a lower court agreed.

But the U.S. Court of Appeals for the Federal Circuit, which was established to specialize in patent cases, said the combination was not obvious under its test that looked at whether some "teaching, suggestion or motivation" had anticipated it.

Kennedy said the appeals court's test was helpful but too rigidly applied.

Thomas said the court's ruling makes many existing patents vulnerable to court challenge because they were issued according to a standard the justices have now rejected. The KSR and MedImmune cases, which allowed companies that license technology to challenge the validity of the underlying patent, mean far more uncertainty for patent holders.

In particular, he predicted that generic drug makers would increasingly sue pharmaceutical companies.

Though the court has heard a series of patent disputes during the past two years, the KSR case is unique because it addresses the nature of patents themselves rather than questions about how patent disputes are litigated and resolved.

"KSR had to do with the fundamental issue that affects all patents: whether a patent should be issued in the first place. That touches all patents," said George Best, a patent expert and partner at the Foley & Lardner law firm who did not represent the parties involved in the three cases.

The case could "change the rules of the game from the way they've been for the last 20 years or so," he said, adding that the Supreme Court was not trying to set new law but rather saw its task as reining in the lower appeals court. Other patent lawyers and specialists also called the rulings yesterday the latest rebuke to the federal circuit.

Though the Supreme Court's decision in *KSR* was focused on the specific case -- "the most detailed technical discussion that's come out of the Supreme Court since the 19th century," according to Thomas -- the justices were intent on sending a broader message.

Microsoft v. AT&T centered on whether Microsoft's liability for infringing AT&T's patent on a speech processor extended to computers manufactured overseas and loaded with Windows software copied abroad. "Our answer is no," Ginsburg wrote.

She said that because the master disk Microsoft sends from the United States is never installed on any of the foreign-made computers, the law prohibiting the exportation of patented "components" has not been violated.

The court's decisions come as an effort to retool the patent system is gaining momentum on Capitol Hill. Members of Congress are grappling with some of the same basic issues about patent rights that the justices faced in these two cases, in particular the question of whether the protection for patents has grown too strong and the penalty for violating them too costly.

As part of the overhaul drive, many high-tech companies have been urging Congress to make clear that U.S. patent law cannot be applied to activities outside the country. But the court's decision seems to settle that.

"Today's Supreme Court decision is important for the entire information technology industry, adding clarity and balance to our patent system," said Brad Smith, Microsoft's general counsel.

Though the Microsoft case turned on a relatively narrow legal issue, Smith said the ruling was crucial for the future because it could affect the country's most innovative industries, in particular the computer and biotechnology sectors.

Stifel Nicolaus, a research firm specializing in technology and telecommunications, said in a report yesterday that a ruling in favor of AT&T could have caused far-reaching harm to other companies.

"The Federal Circuit decision would create massive liability for high-tech firms operating in the United States, including biotech, semiconductor, software and Internet companies that rely on information created in the United States that is transferred abroad by computer code," the research firm wrote.

Patent experts agreed that the ruling also could be relevant to biotech firms, such as those producing genetically engineered cell lines that are sent overseas to be converted into proteins for commercial use.

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EXHIBIT C

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

VISION BIOSYSTEMS (USA) TRADING INC. Plaintiff, v. VENTANA MEDICAL SYSTEMS, INC. Defendant.	)	Civil Action No. 03 CV 10391 GAO

EXPERT REPORT OF DOUG KOEBLER REGARDING U.S. PATENT NO. 6,352,861

1. I, Doug Koebler, submit this report on behalf of Vision BioSystems, Inc. ("Vision"). I have been retained on behalf of Vision to provide expert testimony on the design, operation, and development of automated systems that process specimens for diagnosis in general, and, in particular, on a comparison of certain claims of U.S. Patent No. 6,352,861 ("the '861 patent") and the disclosures of certain prior art documents which predate the '861 patent.

A. Background Information and Qualifications

2. I am currently the Vice President of Engineering for Automated Cell, Inc. My work involves the design and development of an automated system to search for antibodies against cancer cell lines. As part of my responsibilities, I manage software and image processing professionals, write software for control of the instrumentation, and maintain a data transfer network to develop large scale image processing. The instruments that we are currently using were designed and built by me in collaboration

with Carnegie Mellon University and the University of Pittsburgh. I am currently working on further automation of the instruments.

3. In addition to my responsibilities at Automated Cell, I am an adjunct professor of engineering physics at Seton Hill University.

4. I am a member of the American Society of Mechanical Engineers ("ASME"). In May of 2004, I will become the local chairman of that organization. In 2000-2001, the local ASME chapter named me Engineer of the Year. I have been a member of the American Association of Physics Teachers.

5. I received a B.S. degree in education, specializing in physics, from California University of Pennsylvania in 1973. I earned a B.S. in mechanical engineering from the University of Pittsburgh in 1979 and an M.S. in mechanical engineering from Carnegie Mellon University in 1987.

6. I taught high school physics from 1973 - 1976.

7. From 1976 to 1978, I was a systems engineer for Thermox Instruments.

8. From 1979 to 1983, I was a project engineer for Bacharach Instruments.

9. From 1984 to 1988, I worked for Fisher Scientific. I was a group leader for histology product design. I designed histology products, tissue processors, slide stainers, and immunodiagnostic and DNA stainers.

10. From 1989 - 1996, I was the engineering manager for Suprex Corporation, a company which builds supercritical fluid instrumentation.

11. In 1997, I joined Automated Cell, Inc., where I am currently employed.

12. I am a named inventor on seven patents, and three patent applications pending before the United States Patent Office. Among the patents for which I am a

named inventor is U.S. Patent Number 5,023,187 on "Method and Device for Accelerated Treatment of Thin Sample on Surface."

13. A copy of my most recent resume, which includes a list of publications I have authored including U.S. patents and patent applications in which I am a named inventor, is attached as Exhibit A to this report.

14. I expect to testify at trial on matters set forth in this report. I also may testify at trial regarding other matters which may be raised in the reports of other expert witnesses or at trial. In preparing this report, I have reviewed documents provided to me by Vision's counsel. A list of these documents is attached to this report as Exhibit B. The opinions set forth in this report are based upon my professional training and experience and the documents I have reviewed. I reserve the right to supplement this report.

15. I have not testified as an expert at trial or by deposition in the last four years.

16. I am being compensated for my time in this matter at the rate of $200 per hour. My compensation is not dependent upon the outcome of this lawsuit.

B. A Person of Ordinary Skill in the Art

17. A person having ordinary skill in the art to which the subject matter of the '861 patent relates would have a bachelor's degree or equivalent in mechanical engineering, electrical engineering, or computer science. Such a person would have significant experience in the design of instruments which automate the preparation of samples for diagnosis. A person of ordinary skill in the art would also have at least a general understanding of bar code technology and its use in automated systems that

process specimens for diagnosis.

C. Vision's Bond Instruments

18. I have been informed by counsel for Vision as to how Vision's instruments – the Bond™-X and the Bond™-maX (collectively, "the Bond instruments") – operate.

19. The Bond instruments stain tissue samples carried on slides using a robotic pipetter to transfer reagents from reagent containers to the slides.

20. The reagent containers (although not the bulk reagent containers) include two bar codes: top bar codes and side bar codes. The top bar codes are read by a bar code reader on the instrument and encode only a unique package identifier ("UPI"). The UPI is associated within a database with reagent identification data that was entered by the instrument operator prior to placing the container in the instrument. The operator enters the reagent identification data into the database and associates the identification with the UPI by scanning the container's side bar code with a handheld scanner or by keying identification data into the instrument computer. The reagent identification is not encoded into the top bar code.

21. Slides processed by the Bond instruments include a bar code label. The information encoded into the slide bar code is a unique identifier that is correlated with data, including sample identification and protocol information, that was entered by the instrument operator prior to placing the slide into the instrument. Neither the identity of the protocol nor the actual protocol information, which would include an identification of the reagents to be applied to the slide as well as the sequence with which the reagents should be applied, is encoded into the slide bar code.

22. Prior to placing a slide into the Bond instrument, the operator must manually enter into the instrument computer sample identification data as well as protocol identification data for that slide. The instrument computer assigns a slide ID to the slide. After the instrument operator has entered all necessary data for the slide and activates the label print button, the instrument computer assigns a unique label ID that is encoded in the bar code printed on the label. The label ID is used only once by the system. Should it become necessary to reprint the label, the slide ID would remain the same, but the label ID (and hence the bar code) associated with that slide ID would be changed to a new unique label ID regardless of whether or not any of the operator-input data was changed.

23. I am informed that Ventana contends that the Bond instruments infringe claims 1, 2, 3, 5, 6, and 8 of the '861 patent. The opinions and analysis set forth in this report are limited to those claims.

D. Prior Art Documents

24. In analyzing whether or not the elements recited in claims 1, 2, 3, 5, 6, and 8 of the '861 patent were described in documents that predate the filing date of the '861 patent, I considered the documents listed in Exhibit B. Of the documents listed in Exhibit B, I attach as Exhibit C copies of the following documents which I found to be particularly relevant.

a. Japanese patent publication number 55-107957 entitled "Method of Analyzing Blood Profiles," filed February 13, 1979, published August 19, 1980, including two English translations of the document ("JP '957").

In the device described in this publication, substances, such as blood samples and

dying reagents, are dispensed on slides. A sample container holding the blood specimen includes a specimen code label that indicates a specimen number. A blood sample is transferred from the container to slides having a bar code. The bar code on the slide and the specimen code on the sample container are both read by code readers and are linked to each other and stored in a storage device. The slide is then stained using a dyeing procedure. Following the dyeing procedure, the slide is observed through a microscope for diagnosis. The slide is identified by the link between its bar code and the sample container bar code.

b. US Patent Number 4,528,159, "Automated Analysis Instrument System," filed July 20, 1982, Date of Patent July 9, 1985 ("Liston '159").

c. Driscoll et al., "Discrete Automated Chemistry System with Tableted Reagents," Clinical Chemistry, Vol. 29. No 9, 1983, pp. 1610-1615. ("Driscoll et al.").

After reading Liston '159 and Driscoll et al., it became clear to me that they are describing the same instrument. In the instrument described, which I will refer to as the "Liston/Driscoll instrument," patient samples are provided in tubes. Specific tests are selected by a laboratory technician on a cathode-ray tube display, and sample-container bar codes are automatically printed for each sample and affixed to the sample container. The sample bar codes are read by a bar code reader on the instrument, and the instrument computer correlates each sample bar code ID with the specified tests for that sample. Using a bar code ID on each sample container allows the sample container to be positioned randomly within the instrument. There is a reagent dispenser carousel which holds the reagent dispenses. The dispensers carry reagents in tablet form, which are

activated by the addition of further reagents and diluents and mixed by ultrasonics. The dispensers in this carousel include optical codes that are read by an optical code reader to identify the reagents contained in the dispensers, thereby allowing loading of the dispensers randomly.

d. Tilzer, Lowell L., and Jones, R., "Use of Bar Code Labels on Collection Tubes for Specimen Management in the Clinical Laboratory," Archives of Pathology and Laboratory Medicine, Vol. 112, Dec. 1988, pp. 1200-1202 ("Tilzer").

This article discusses the use of bar codes on medical laboratory equipment. In particular, Tilzer describes "a method using an LIS [(laboratory information system)]-generated bar code label that allows for automatic identification of specimens and processing of tests on a random-access chemistry analyzer." Tilzer, p. 1202. Tilzer specifically discusses the use of bar codes on evacuated collection tubes for blood which allows for random access with a chemistry analyzer. The analyzer has a 30 test menu. The system is totally integrated with the LIS in conjunction with a random-access chemistry analyzer for "stat" as well as routine testing. Bar-coded collection tubes are loaded directly onto the analyzer. The bar codes are automatically read, specimens identified, and up to 30 tests performed on each sample. The specimens could be loaded on the analyzer in any order. The article points out that the benefits of the device include reducing errors and increasing the number of samples processed through the lab. The article makes reference to the use of the bar code system for handling urine and other body fluids in a similar manner. Furthermore, the article states that the system can also be used for automated instruments in other sections of the laboratory, such as hematology, blood bank, and microbiology.

e. Keenan, Robert, L., et al., "Patient Identification in an Automated Clinical Laboratory System," IEEE Frontiers of Engineering in Health Care, 1982, pp. 15-18. ("Keenan et al.")

This article describes a patient ID system that automates processing of blood specimens to produce chromosome preparations on microscope slides. Bar codes are placed on blood sample tubes, culture trays, and microscope slides. Patient and sample information are linked to bar codes attached to the specimen tube, culture trays, and the microscope slides by a computer. A data table listing names, additional patient data, and all ID numbers read is generated.

f. Japanese patent publication number 63-61165 entitled "Reagent Identification Apparatus in Automated Chemical Analyzer," filed September 2, 1986, published March 17, 1988, including an English translation of the document, ("JP '165")

This document describes a chemical analyzer in which reagents are identified by the instrument computer by means of bar codes placed on the reagent containers.

g. United States Patent No. 4,159,875 to Hauser, issued July 3, 1979.

This patent describes a slide holder suitable for use in an automated differential blood cell classifier. The slide holder includes a bar code for encoding machine-readable information, such as identification information.

E. Analysis of the '861 Patent

25. I have reviewed the '861 patent, and I understand the technology described. I have reviewed claims 1, 2, 3, 5, 6, and 8, which I understand are at issue in this lawsuit.

26. Claim 1 of the '861 patent recites:

> A method of dispensing reagents onto a slide, the method comprising the steps of:
>
> providing at least one reagent container;
>
> providing at least one slide on a slide support;
>
> automatically identifying the reagent container using a computer;
>
> automatically determining whether reagent in the reagent container should be dispensed onto the slide; and
>
> dispensing the reagent in the reagent container onto the slide based on the determination of whether the reagent in the reagent container should be dispensed onto the slide,
>
> wherein the step of automatically determining whether reagent in the reagent container should be dispensed onto the slide includes the steps of:
>
> providing a bar code reader;
>
> reading a slide bar code placed on the slide using the bar code reader thereby acquiring slide information, the slide information indicating reagents to be applied to the slide; and
>
> sending the slide information to the computer.

27. In my opinion, if claim 1 of the '861 patent covers the Bond instruments, as Ventana alleges, then every element of claim 1 is described in prior art documents I have reviewed.

28. Claim 1 is directed to: "[a] method of dispensing reagents onto a slide." JP '957 describes a method of dispensing substances onto a bar coded slide. The Liston/Driscoll instrument performs a method for dispensing reagents.

29. The first element of claim 1 is "providing at least one reagent container."

The Liston/Driscoll instrument includes tableted reagent dispensers carried on a rotatable dispenser carousel. Liston '159, col. 5, lns. 44-45; Driscol et al., p. 1609.

30. The next element of claim 1 is "providing at least one slide on a slide support." The Liston/Driscoll instrument includes sample containers, e.g., collection tubes, carried on a loading carousel. Liston '159, col. 5, lns. 59-61. The staining system described in JP '957 includes specimen slides 11.

31. The next element of claim 1 is "automatically identifying the reagent container using a computer." Driscoll et al. describes a corresponding aspect of the Liston/Driscoll instrument: "[t]he tablet-dispenser carousel includes an optical code reader to identify the reagent contained in each dispenser. This feature allows the loading of dispensers randomly (i.e., without a programmed sequence) into the carousel." Driscoll, et al., p.1609.

32. The next element of claim 1 is "automatically determining whether reagent in the reagent container should be dispensed onto the slide." Driscoll et al. explains that in the Liston/Driscoll instrument, "[t]he analyzer's data system automatically prints a bar code to be applied to the sample container at the time test requests are entered for the sample." Driscoll, et al., p. 1610. The bar code reader of the Liston/Driscoll instrument identifies the patient sample, which is correlated with the test requisition for this sample that has already been entered into the instrument computer system by the laboratory technician. Liston '159, col. 6, lns. 30-36. Liston also explains that the sample container and the reaction container can be the same container. Liston '159, col. 4, ln. 63 - col. 5, ln. 2. A person of ordinary skill in the art would recognize that a slide is an example of a sample container that is also a reaction container.

33. The next element of claim 1 is "dispensing the reagent in the reagent container onto the slide based on the determination of whether the reagent in the reagent container should be dispensed onto the slide." In the Liston/Driscoll instrument, when the bar code label on the sample container is scanned by the bar code reader, the appropriate reagent is dispensed in the reaction cuvette. Liston '159, col. 6, lns. 30-36, col. 7, lns. 3-9; Driscoll et al., pp. 1610-1611.

34. The next paragraph of claim 1 – "wherein the step of automatically determining whether reagent in the reagent container should be dispensed onto the slide includes the steps of" – introduces the elements which further define the "automatically determining" step.

35. The next element of claim 1 is "providing a bar code reader." The Liston/Driscoll instrument includes a bar code reader. Liston '159, Fig. 1; col. 5, lns. 61-62.

36. The next element of claim 1 is "reading a slide bar code placed on the slide using the bar code reader thereby acquiring slide information, the slide information indicating reagents to be applied to the slide." Liston '159 explains that in Liston/Driscoll instrument,

> [t]he transfer carousel 64 then indexes around to bar code reader 66 which identifies the patient sample. This sample identity is fed to an instrument control microprocessor (not shown) which correlates this information with the test requisition for this sample that has already been entered into the instrument computer system by the laboratory technician.

Liston '159, col. 6, lns. 30-36. Driscoll further explains that "[t]he analyzer's data system automatically prints a bar code to be applied to the sample container at the time

test requests are entered for the sample. . . . [T]he sample container's bar code is read, which initiates tablet dispensing for the requested tests." Driscoll et al., pp. 1610-1611. JP '957 teaches the use of bar codes on sample slides and sample containers for correlating a slide identification with a sample identification when a sample is transferred from the container to the slide.

37. The last element of claim 1 is "sending the slide information to the computer." In the Liston/Driscoll instrument, the sample identity is fed to an instrument control microprocessor which correlates the identity information with the test requisition for the sample that has already been entered into the instrument computer system by a laboratory technician. Liston '159, col. 6, lns. 30-36.

38. In the Liston/Driscoll instrument it is contemplated that the identity of the reagents to be applied is not encoded in the slide bar code. As described in Liston '159, a patient sample identifier is encoded in the slide bar code. The patient sample, after being read by the bar code reader, is correlated by the system computer with the test requisition – which specifies the reagents to be applied – previously entered by the laboratory technician. In this regard, the Liston/Driscoll instrument functions in a manner that is identical to the manner in which the Bond instruments operate. In the Bond instruments, the slide bar code is encoded with only a unique ID, and the computer of the Bond instrument correlates the unique bar code ID with the slide ID and correlates the slide ID with the protocol data that was entered by the operator. Therefore, if claim 1 covers the Bond instruments, as alleged by Ventana, then Liston '159, Driscoll et al., and JP '957 describe all of the elements of claim 1.

39. As demonstrated above, Liston '159, Driscoll et al., and JP '957 describe

all the elements of claim 1. While I recognize that the Liston/Driscoll instrument does not use slides, it is clear to me that it would have been obvious to a person of ordinary skill in the art to have employed the methodology embodied in the Liston/Driscoll instrument in a slide preparation process.

40. From my own training and experience, I know that the automation and use of bar codes described in Liston '159 and Driscoll et al. would be readily applicable to a slide preparation process. Furthermore, Liston '159 describes the dual use of the sample container for both collecting the sample and performing the reaction. Liston '159, col. 4, ln. 64 - col. 5, ln. 2. A slide is an example of such a container. Tilzer also describes the use of bar codes on containers used for both sample collection and as reaction vessels in a chemical analyzer. Tilzer et al., p. 1200. Furthermore, the use of bar codes on slides for automated identification and processing was known well before the '861 filing date, as described, for example, in JP '957, Hauser '875, and Keenan et al.

41. Tilzer et al. also explains that the system described can also be used for automated instruments in other sections of the laboratory such as hematology, blood bank, and microbiology. Tilzer et al., p. 1202. That is, the technique described is applicable to instruments that process slides. As Tilzer, a 1988 article, explains, "[b]ar code labels generated next to an instrument and used to identify patient samples are becoming commonplace." Tilzer et al., p. 1200.

42. The advantages of using bar codes in automated sample preparation instruments were known to persons of ordinary skill in the art when the '861 patent was first filed, and these advantages are also described in a number of the documents I reviewed. For example, Liston '159 explains: "[a]nother significant advantage of the

automated analysis system of the present invention is that it permits the effective use of a microprocessor-controlled loading and transfer assembly for presenting to the analyzer containers having the samples to be tested." Liston '159, col. 4, lns. 49-53. Driscoll et al explains that "[s]ample entry is totally random" and that bar codes provide "positive sample identification." Driscoll et al. at 1609. JP '957 explains that the invention facilitates automation of the slide preparation and examination process, that the glass slides can be arranged randomly, and that bar code identification makes it possible to dye many samples in a group. The fact that these documents describe similar advantages that can be achieved with bar codes on different types of sample containers – i.e., test tubes, cuvettes, or slides – demonstrates that the advantages, as well as the methodology that achieves the advantages, are equally applicable to an instrument that processes microscope slides as well as an instrument that processes test tubes and cuvettes.

43. Claim 2 of the '861 patent recites:

> The method of claim 1 wherein the slide bar code identifies a slide sample placed on the slide and identifies a sequence of reagents for the slide sample.

44. In my opinion, if claim 2 covers the Bond instruments, as Ventana alleges, then every element of claim 2 is described in prior art documents I have reviewed.

45. As Liston '159 explains:

> [t]he transfer carousel 64 then indexes around to bar code reader 66 which identifies the patient sample. This sample identity is fed to an instrument control microprocessor (not shown) which correlates this information with the test requisition for this sample that has already been entered into the instrument computer system by the laboratory technician.

Liston '159, col. 6, lns. 30-36. Similarly, Driscoll et al. explains: "[t]he analyzer's data

system automatically prints a bar code to be applied to the sample container at the time test requests are entered for the sample. . . . [T]he sample container's bar code is read, which initiates tablet dispensing for the requested tests." Driscoll et al., pp. 1610-1611. Thus, in the Liston/Driscoll instrument, the sample bar code identifies the patient sample, and the sample identity is used to determine the test (i.e., sequence of reagents) that has been requested for the sample. JP '957 teaches the use of bar codes on sample slides and sample containers for correlating a slide identification with a sample identification when a sample removed from the container is placed on the slide.

46. Thus, all the elements of claim 2 are described in prior art documents I reviewed, and, moreover, combining the teachings of these documents would have been obvious to a person of ordinary skill in the art for the reasons explained with respect to claim 1 above.

47. Claim 3 of the '861 patent recites:

> The method of claim 1 further comprising the steps of:
> determining position information for the slide; and
> sending the position information to the computer.

48. In my opinion, if claim 3 covers the Bond instruments, as Ventana alleges, then every element of claim 3 is described in prior art documents I have reviewed.

49. In the Liston/Driscoll instrument, cuvettes are indexed through the instrument every 5 seconds. Driscoll et al., p. 1609; Liston '159, col. 6, lns. 61-64. Thus, the position of each cuvette can be determined by the time lapsed since it was at a known position, such as the reagent dispensing station. Since the cuvettes move past a number of optical read stations and other instruments, it is necessary for the system computer to track the position of each cuvette so that the cuvette at any particular station

can be identified.

50. Thus, all the elements of claim 3 are described in prior art documents I reviewed. Combining the teachings of these documents would have been obvious to a person of ordinary skill in the art for the reasons explained with respect to claim 1 above.

51. Claim 5 recites:

> A method of dispensing reagents onto a slide, the method comprising the steps of:
>
> providing a plurality of reagent containers in a reagent support, each of the reagent containers having a reagent barcode;
>
> providing at least one slide on a slide support, the slide having a bar code;
>
> providing a bar code reader;
>
> reading the bar codes on the reagent containers;
>
> determining reagents in the reagent containers based upon the reading of the bar codes on the reagent containers;
>
> reading the slide bar code on the at least one slide;
>
> determining a sequence of reagents to be applied on the at least one slide based upon the reading of the slide bar code on the slide; and
>
> dispensing the reagents in the reagent containers based upon the sequence of reagents to be applied.

52. In my opinion, if claim 5 covers the Bond instruments, as Ventana alleges, then every element of claim 5 is described in prior art documents I have reviewed.

53. Claim 5 is directed to: "A method of dispensing reagents onto a slide." JP '957 describes a method of dispensing substances onto a bar coded slide. The

Liston/Driscoll instrument performs a method for dispensing reagents.

54. The first element of claim 5 is "providing a plurality of reagent containers in a reagent support, each of the reagent containers having a reagent barcode." The Liston/Driscoll instrument includes tableted reagent dispensers carried on a carrousel. An optical reader on the carrousel identifies the reagents contained in each container. Liston '159, col. 5, lns. 44-45. Driscoll et al., p. 1609. Driscoll et al. does not specifically describe reagent bar codes but describes an "optical code reader" to identify the reagent contained in each dispenser. Driscoll et al., p. 1609. Driscoll et al. also describes that the reagents can be positioned randomly on the carousel. Driscoll et al., p. 1609. Thus the reagent container must have a code on it that is read by the optical code reader to identify the reagent. A person of ordinary skill in the art would appreciate that a bar code is a type of optical code.

55. The next element of claim 5 is "providing at least one slide on a slide support, the slide having a bar code." The Liston/Driscoll instrument includes sample containers with bar codes. Liston '159, Fig. 2; col. 5, lines 59-61; Driscoll, et al. at 1610. JP '957 describes bar-coded glass slides on an instrument that prepares samples for analysis.

56. The next element of claim 5 is "providing a bar code reader." Liston '159 describes that the Liston/Driscoll instrument includes a bar code reader. Liston '159 Col. 5, lines 61-62. JP '957 describes a bar code reader.

57. The next two elements of claim 5 are "reading the bar codes on the reagent containers; [and] determining reagents in the reagent containers based upon the reading of the bar codes on the reagent containers." In the Liston/Driscoll instrument as

described in Driscoll et al., "[t]he tablet-dispenser carousel includes an optical code reader to identify the reagent contained in each dispenser. . . . Each reagent is correlated with a specific carousel position in the system's memory; when a reagent is requested, the carousel rotates to the appropriate position for dispensing that reagent into the cuvette." Driscoll et al. at p. 1609. Similarly, JP '165 describes an instrument in which reagents are identified by bar codes placed on the reagent containers.

58. The next two elements of claim 5 are "reading the slide bar code on the at least one slide; [and] determining a sequence of reagents to be applied on the at least one slide based upon the reading of the slide bar code on the slide." In the Liston/Driscoll instrument, the bar code label on the patient sample is read by the bar code reader. Liston '159, col. 5, lns. 61-62. Moreover, Liston '159 explains:

> The transfer carousel 64 then indexes around to bar code reader 66 which identifies the patient sample. This sample identity is fed to an instrument control microprocessor (not shown) which correlates this information with the test requisition for this sample that has already been entered into the instrument computer system by the laboratory technician.

Liston '159, col. 6, lns. 30-36. Similarly, Driscoll et al. discloses that "[a]t five positions before the sampling station, the sample container's bar code is read, which initiates tablet dispensing for the requested tests." Driscoll, et al. at 1610-1611. JP '957 teaches the use of bar codes on sample slides and sample containers for correlating a slide identification with a sample identification when a sample removed from the container is placed on the slide.

59. The last element of claim 5 is "dispensing the reagents in the reagent containers to be applied." Liston '159 describes that:

> The microprocessor causes the proper reagent to be dispensed [into a reaction cuvette] from one of the thirty-two different tableted reagent dispensers 40 that can be accommodated by dispenser carousel 42, or the multiple liquid reagents that can be accommodated by diluent/liquid reagent dispenser 50, in response to the patient sample identification by bar code reader 66.

Liston '159, col. 7, lines 3-9. Liston '159 further explains the benefits that can be achieved by conducting reactions directly in the sample collection container. Liston 159, col. 4, ln. 63 - col. 5, ln. 2.

60. In the Liston/Driscoll instrument, it is contemplated that the identity of the reagents to be applied is not encoded in the slide bar code. As described in Liston '159, a patient sample is encoded in the slide bar code. The patient sample, after being read by the bar code reader, is correlated by the system computer with the test requisition – which specifies the sequence of reagents to be applied – previously entered by the laboratory technician. In this regard, it is contemplated that the Liston/Driscoll instrument functions in a manner that is identical to the manner in which the Bond instruments operate. In the Bond instruments, the slide bar code is encoded with only a unique ID, and the computer of the Bond instrument correlates the unique bar code ID with the slide ID and correlates the slide ID with the protocol data that was entered by the operator. Therefore, if claim 5 covers the Bond instruments, as alleged by Ventana, then Liston '159, Driscoll et al., and JP '957 describe all of the elements of claim 5.

61. As demonstrated above, Liston '159, Driscoll et al., and JP '957 describe all the elements of claim 5. While I recognize that the Liston/Driscoll instrument does not use slides, it is clear to me, for reasons discussed above with respect to claim 1, that it would have been obvious to a person of ordinary skill in the art to have employed the

methodology described in Liston '159 and Driscoll et al. in a slide preparation process.

62. Claim 6 recites :

> The method of claim 5 further comprising the steps of: determining position information for the reagent containers; and sending the position information to the computer.

63. In my opinion, if claim 6 covers the Bond instruments, as Ventana alleges, then every element of claim 6 is described in prior art documents I have reviewed.

64. In the Liston/Driscoll instrument, "[e]ach reagent is correlated with a specific carousel position in the system's memory; when a reagent is requested, the carousel rotates to the appropriate position for dispensing that reagent into the cuvette." Driscoll, et al. at 1609.

65. Thus, all the elements of claim 6 are described in prior art documents I reviewed. Combining the teachings of these documents would have been obvious to a person of ordinary skill in the art for the reasons explained above.

66. Claim 8 recites:

> The method of claim 5 further comprising the steps of: determining position information for the at least one slide; and sending the position information to the computer.

67. In my opinion, if claim 8 covers the Bond instruments, as Ventana alleges, then every element of claim 8 is described in prior art documents I have reviewed.

68. In the Liston/Driscoll instrument, cuvettes are indexed through the instrument every 5 seconds. Thus, the position of each cuvette can be determined by the time lapsed since it was at a known position, such as the reagent dispensing station.

69. Thus, all the elements of claim 8 are described in prior art documents I

reviewed. Combining the teachings of these documents would have been obvious to a person of ordinary skill in the art for the reasons explained above.

70. Thus, for the reasons explained above, if claims 1, 2, 3, 5, 6, and 8 of the '861 patent cover the Bond instruments, as Ventana alleges, then I believe that all elements of these claims are described in Liston '159, Driscoll et al., and JP '957.

Dated: 4/8/2004

Doug Koebler

EXHIBIT D

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

VISION BIOSYSTEMS (USA) TRADING, INC., Plaintiff, v. VENTANA MEDICAL SYSTEMS, INC., Defendant.	CIVIL ACTION NO. 03-CV-10391-GAO

EXPERT REPORT OF ANDRE SHARON, Ph.D.

1. I am a Professor of Manufacturing Engineering at Boston University and the Executive Director of the Fraunhofer Center for Manufacturing Innovation. Prior to joining the Fraunhofer Center for Manufacturing Innovation and Boston University, I co-founded and served as the Executive Officer of the Massachusetts Institute of Technology Manufacturing Institute. I also served as the Associate Director of the Massachusetts Institute of Technology Laboratory for Manufacturing and Productivity.

2. I received my Bachelors of Science degree from the Polytechnic Institute of New York, and my Masters of Science and Doctor of Philosophy degrees from the Massachusetts Institute of Technology. A copy of my resume is attached as Exhibit A, and a list of my publications is attached as Exhibit B.

3. I have twenty years of academic and industrial experience developing and deploying state-of-the-art automation to industry, ranging from sub-micron, high-precision machinery for optoelectronics, biotechnology, and semiconductor manufacturing to high-speed

assembly of consumer products. I am the Editor-in-Chief of the International Journal, Robotics and Computer Integrated Manufacturing. I am a named inventor on six issued United States patents.

4. I have been retained by the firm of Wilson Sonsini Goodrich & Rosati as a consultant in connection with the above-captioned lawsuit. For my work on this matter, I am being compensated at my consulting rate of $250 per hour for non-testifying time, and $350 per hour for deposition and courtroom appearances. I have not testified as an expert at trial or by deposition within the preceding four years.

5. If called as an expert witness in this matter, I anticipate that my testimony may concern the matters addressed below. My anticipated testimony may be affected by the production of additional information and/or positions plaintiff takes on the topics set forth in this report. I have been informed that plaintiff may communicate at least some of those positions to defendant some time after this report is prepared, such as in the form of deposition testimony to be given by its experts. After I have an opportunity to review those materials, I may amend this report.

6. In connection with formulating the opinions set forth in this report, I have reviewed at least the following material: U.S. Patent No. 6,352,861 ("the '861 patent") and portions of its prosecution history; the Expert Report of Doug Koebler Regarding U.S. Patent No. 6,352,861 ("the Koebler Report"), and the materials attached to that report; Keenan et al., *Patient Identification in an Automated Clinical Laboratory System*, IEEE Frontiers of Eng. in Health Care, 15-18 (1982) ("Keenan"); Tilzer et al., *Use of Bar Code Labels on Collection Tubes for Specimen Management in the Clinical Laboratory*, Arch. Pathol. Lab. Med., 112:1200-1202 (Dec. 1988) ("Tilzer"); Hauser, *Specimen Holder*, U.S. Patent No. 4,159,875 (1979) ("Hauser");

English translations of Kojima et al., *Analyzing Method of Blood Image*, Japanese Pat. App. Pub. No. 55-107957 (1980) ("JP '957"); Liston, *Automated Analysis Instrument System*, U.S. Patent No. 4,528,159 (1985) ("Liston"); Driscoll et al., *Discrete Automated Chemistry System with Tableted Reagents*, Clin. Chem., 29:1609-1615 (1983) ("Driscoll"); English translations of Japanese Pat. App. Pub. No. 63-61165 (1988) ("JP '165"); and the Expert Report of David G. Hicks, M.D.

7. The system described in the '861 patent pertains to the field of machine design and automation. A person of ordinary skill in the art in that field would typically have a bachelor's degree or equivalent in mechanical engineering, and would likely require assistance from an electrical engineer and/or a computer scientist for the development of the often-required software and controls. In addition, developing successful automation requires consultation with the intended customer or end user, which in the case of the '861 patent would be a pathologist. While the engineer described above, in 1990, would have been aware of the use of bar codes for identification purposes, he/she would most likely not have experience with the use of bar codes in driving automated processes.

8. I have read the references cited in the Koebler Report. JP '957 describes a batch processing apparatus for the analysis of blood samples smeared onto glass slides. The bar codes are only used for ensuring correct matching of samples to the slides. A cassette containing a batch of individually bar coded slides is immersed in solution tanks. The bar code on a slide is not used in any way to determine what treatment is to be applied to the individual slide.

9. Liston describes an apparatus in which samples from bar coded sample containers are placed into cuvettes (in which reagents were previously dispensed), photometrically analyzed, and then disposed. This system does not make use of slides, and furthermore, uses a

separate, non-bar coded reaction chamber (cuvette) for the treatment of the sample. Additionally, Liston does not disclose bar codes on the reagent containers, nor optical code readers to identify the reagent containers.

10. Driscoll is a journal publication that describes a somewhat modified version of the apparatus described in Liston.

11. Tilzer describes an approach to bar coding specimen collection tubes that are presented to chemical analyzers for testing. Bar codes on the collection tubes are used to identify the samples on which up to 30 tests can be performed. This approach does not use or even imply the use of slides for specimen collection, and furthermore, as in Liston and Driscoll, does not disclose bar codes on the separate reaction chamber used for the treatment of the samples.

12. Keenan discusses patient I.D. quality control in a semi-automated system for processing human blood. The approach described uses batch processing, in which bar codes on slides are used for identification purposes only.

13. JP '165 describes a reagent identification strategy based on bar code identification on reagent containers. It does not mention the use of slides nor does it discuss any treatment process.

14. Hauser describes a specific slide holder in which slides may be bar coded and optically read. It does not mention dispensing reagents nor does it discuss any treatment process.

15. Mr. Koebler, in his report, compares the language of the '861 patent claims with Liston, Driscoll, and JP '957. There are a number of differences between these references and the '861 patent, which I discuss below.

The Liston and Driscoll References

16. Liston and Driscoll fail to disclose the preamble of claims 1 and 5 of the '861 patent, which are directed to "a method of dispensing reagents onto a slide." Instead, both Liston and Driscoll disclose dispensing tableted reagents into cuvettes. Cuvettes do not constitute slides, and in fact, require significantly different processing techniques than dispensing onto slides, as I discuss later in this report.

17. Liston and Driscoll also fail to disclose "providing at least one slide on a slide support," as required by claims 1 and 5. As Mr. Koebler asserts in paragraph 30 of his report, these references disclose "sample containers, e.g., collection tubes, carried on a loading carousel." Any implication that the sample containers described by Liston and Driscoll could include slides once again fails to address the significantly different processing techniques associated with each. Furthermore, neither Liston nor Driscoll disclose the dispensing of reagents into these "sample containers." Rather, they describe dispensing of reagents into separate reaction chambers, namely, cuvettes.

18. Claim 1 also requires "automatically determining whether reagent in the reagent container should be dispensed onto the slide" and "dispensing the reagent in the reagent container onto the slide based on the determination of whether the reagent in the reagent container should be dispensed onto the slide." Claim 5 requires "reading the slide bar code on the at least one slide; determining a sequence of reagents to be applied on the at least one slide based upon the reading of the slide bar code on the slide; and dispensing the reagents in the reagent containers based upon the sequence of reagents to be applied." Liston and Driscoll disclose dispensing a tableted reagent and diluent into a reaction chamber consisting of a cuvette. (Liston, 5:44-55; Driscoll, p. 1609-10) Subsequently, a portion of the sample is transferred from

the sample container into the reaction chamber, where it is allowed to react with the reagent. (Liston, 6:1-7; Driscoll, p. 1610) This approach is very different from that described in the '861 patent, in which reagents are dispensed onto a sample on a bar coded slide, on which the reaction actually occurs. The '861 patent eliminates the need to transfer the sample from a sample container into a separate reaction chamber (cuvette), as described in Liston and Driscoll. This transfer is generally detrimental to fragile pathology samples, which cannot be easily subdivided and transferred as is done with the bulk transfers in Liston and Driscoll. By eliminating the sample transfer step, the overall system robustness is improved.

19. In paragraph 32 of the Koebler Report, Mr. Koebler asserts that "Liston also explains that the sample container and reaction container can be the same container. Liston '159, col. 4, ln. 63 - col. 5, ln. 2." He makes a similar assertion in paragraph 59. I disagree with Mr. Koebler's interpretation of the cited language. In fact, Liston states in that passage that the sample container can be the same container in which the sample was collected "(*i.e.*, in the case of blood samples, the 'Vacutainer' tube which is commonly used to draw the sera specimen)." It does not state nor imply that the sample container and the reaction container can be the same container.

20. Liston and Driscoll also fail to disclose "reading a slide bar code placed on the slide using the bar code reader thereby acquiring slide information, the slide information indicating reagents to be applied to the slide," as required by claim 1 of the '861 patent, or "the slide having a bar code," as required by claim 5. In intended applications of the '861 patent, it is important to track the treated sample on the slide (where the reaction takes place) throughout the entire staining process, because the treated sample must be subsequently presented to the pathologist for human analysis. This definitive tracking of the treated sample is a crucial aspect

of the '861 patent. In contrast, Liston and Driscoll do not utilize information acquired from reading a bar code on a slide, nor from any bar code on their reaction chamber (cuvette) into which reagents are to be applied. This may be acceptable in their intended applications, in which the reaction chamber is photometrically analyzed (Liston, 6:8-13; Driscoll, p. 1611) and the contents disposed (Liston, 7:50-57; Driscoll, p. 1609).

21. Liston and Driscoll also fail to disclose the requirements of claim 2 of the '861 patent, for the reasons I describe above.

22. Liston and Driscoll also fail to disclose determining position information for the slide, as required by claims 3 and 8 of the '861 patent. Mr. Koebler, in paragraph 49 of his report, refers to the indexing of cuvettes and determination of their position based on "the time lapsed since it was at a known position." This disclosure does not refer to bar coded slides, and in fact, is a much less robust method of tracking in which the cuvette can only be identified while it is in the machine, *i.e.*, the identity of the treated sample would be lost if it were to be removed from the machine. This may be acceptable in their intended application, where the contents of the cuvette are analyzed and disposed. It would not, however, be acceptable in the intended application of the '861 patent, in which the treated sample on the slide must be removed from the machine for human analysis, while maintaining definitive identity (through a bar code on the slide) of the treated sample. Furthermore, in the position identification method used by Liston and Driscoll, the position of the cuvette (hence identity) could be lost if the machine were to experience a fatal error (crashes). This would not be acceptable in pathology applications, in which repetition of the sample acquisition (*e.g.*, biopsy) would be difficult.

The JP '957 Reference

23. The preamble of claims 1 and 5 of the '861 patent are directed to "a method of dispensing reagents onto a slide." While paragraph 28 of the Koebler Report states that JP '957 "describes a method of dispensing substances onto a bar coded slide," in fact, JP '957 does not describe dispensing reagents onto bar coded slides. Rather, it describes the immersion of a cassette of bar coded slides into solution tanks. Immersion is a significantly different process from that of dispensing reagents onto a slide.

24. JP '957 fails to disclose "reading a slide bar code placed on the slide using the bar code reader thereby acquiring slide information, the slide information indicating reagents to be applied to the slide," as required by claim 1 of the '861 patent. JP '957 also fails to disclose a slide bar code that "identifies a sequence of reagents for the slide sample," as required by claim 2, and "determining a sequence of reagents to be applied on the at least one slide based upon the reading of the slide bar code on the slide," as required by claim 5 of the '861 patent. JP '957 does not use information from a bar code on a slide to indicate or identify reagents to be applied. Rather, it works in a batch processing mode in which all slides in the same cassette, regardless of their individual bar codes, are subjected to the same treatments. Thus, the bar code on the slide is only used to correlate the sample with the slide for tracking purposes, and has nothing to do with determining the reagents to be applied.

The Proposed Combination of Liston, Driscoll, and JP '957

25. In paragraph 39 and 40 of the Koebler Report, Mr. Koebler writes that "it would have been obvious to a person of ordinary skill in the art to have employed the methodology embodied in the Liston/Driscoll instrument in a slide preparation process." He makes a similar argument in paragraph 61. I disagree with this conclusion. Mr. Koebler identifies nothing to

suggest that the approach used by Liston and Driscoll could have been applied in a slide preparation process as set forth in claims 1, 2, 3, 5, 6 and 8 of the '861 patent. There are number of design considerations that are quite different between the Liston and Driscoll cuvette reaction chamber and the slides upon which reagents are dispensed and reacted with the sample in the '861 patent.

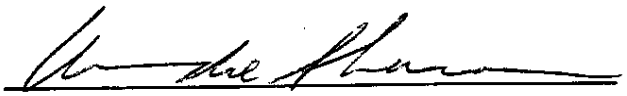
26. The approach used in Liston and Driscoll is based on dispensing tablets/fluids into a bulk container (cuvette) using then-standard tablet and fluid dispensing techniques. Additionally, Liston and Driscoll deal with relatively non-fragile reagent tablets and bulk fluids (including the samples) that can be readily manipulated and mixed, easily lending themselves to automation techniques. By contrast, the '861 patent deals with fragile pathology specimens on a planar slide surface. This introduces challenges that Liston and Driscoll do not address, such as uniform reagent dispensing, evaporation control, and delicately mixing and rinsing reagents on a slide surface. (*See, e.g.*, '861 patent, col. 3-4) Because of these challenges, it would not have been obvious to a person of ordinary skill in the art to employ the Liston and Driscoll approach to a slide preparation process.

27. Mr. Koebler also asserts, in paragraph 40 of his report, that Liston describes "the dual use of the sample container for both collecting the sample and performing the reaction." As pointed out above, there is no such disclosure in Liston. Similarly, Mr. Koebler asserts that Tilzer "also describes the use of bar codes on containers used for both sample collection and as reaction vessels in a chemical analyzer." I find no such disclosure in Tilzer. In fact, Tilzer implies the opposite on page 1201, column 2. He states: "Direct sampling from specimen containers reduces sample handling." Sampling from the specimen container implies that the sampled contents are taken elsewhere, *e.g.*, into a separate reaction chamber.

28. Finally, in paragraph 40 of his report, Mr. Koebler states that "the use of bar codes on slides for automated identification and processing was known well before the '861 filing date, as described, for example, in JP '957, Hauser '875, and Keenan et al." While bar codes on slides had been used for identification and tracking purposes, none of those references disclose bar codes used to determine the specific preparation process on individual slides.

29. In paragraphs 41 and 42 of the Koebler Report, Mr. Koebler points to reported advantages of using bar codes in the prior art that are applicable to slide preparation, thereby suggesting the obviousness of the '861 patent. These advantages, in fact, are not applicable to slide preparation. The first claimed applicable advantage refers to the "microprocessor-controlled loading and transfer assembly" in Liston. In the '861 patent, the sample is never transferred from the original slide during the staining process. In fact, such transfer may be detrimental to the fragile pathology specimen. The second claimed applicable advantage refers to the "totally random" sample entry and "positive sample identification." Unlike the '861 patent, where sample identification is maintained and tracked throughout the entire process using a bar code, Driscoll does not provide bar code identification to track the sample once it is transferred from its original sample container to the cuvette. The third claimed applicable advantage refers to "that the glass slides can be arranged randomly, and that bar code identification makes it possible to dye many samples in a group" in JP '957. In fact, JP '957 describes a batch process in which all slides in a cassette are subjected to the same treatment, regardless of their bar code or arrangement within a cassette.

30. In conclusion, none of the references cited by Mr. Koebler in his report by themselves disclose the entirety of any of claims 1, 2, 3, 5, 6 and 8 of the '861 patent. Furthermore, in my opinion, Mr. Koebler has not made a convincing argument as why it would have been obvious, in 1990, for a person of ordinary skill in the art to combine the cited references to develop the system described in claims 1, 2, 3, 5, 6 or 8 of the '861 patent.



Andre Sharon, Ph.D.

Dr. Andre Sharon
Executive Director
Fraunhofer Center for Manufacturing Innovation
Professor of Manufacturing Engineering
Boston University

In a Nut Shell:

Experience:	20 years of academic and industrial experience developing and deploying state-of-the-art automation to industry, ranging from sub-micron, high-precision machinery for optoelectronics biotechnology, and semiconductor manufacturing to high-speed assembly of consumer products.
Technical Expertise:	Electromechanical Design, Automation Systems, Servo Control
Education:	Ph.D. Mechanical Engineering, Class of '89 Massachusetts Institute of Technology

Professional Biography:

Prof. Andre Sharon has accumulated over 20 years of experience, both industrial and academic, developing and deploying computer-controlled automation equipment for several industries, ranging from sub-micron, high-precision machinery for optoelectronics, biotechnology, and semiconductor fabrication to high-speed assembly of consumer products. As Director of the Fraunhofer Center for Manufacturing Innovation and Professor of Manufacturing Engineering at Boston University, Prof. Sharon works closely with faculty, students and engineers to develop next-generation manufacturing technologies for local and international clients. Drawing upon Fraunhofer's and Boston University's vast research base and working closely with industry, the Center goes beyond the scope of traditional academic research to develop and deploy actual working technologies all the way to the factory floor.

Prior to joining Fraunhofer / Boston University, Prof. Sharon co-founded and served as Executive Officer of the MIT Manufacturing Institute, created to bridge the gap that exists between traditional academic research and the needs of industry. Prof. Sharon led a large program aimed at cost reducing the manufacture of optoelectronics and fiber optic systems through the development of cost-effective packaging, pigtailing and handling equipment. He developed and deployed several machines that greatly reduce the cost of fabricating photonic devices. Additionally, Prof. Sharon has consulted extensively for industry in the area of cost-effective automation.

Prior to joining MIT, Prof. Sharon spent seven years at IBM's T.J. Watson Research Center and IBM's General Technology Division developing manufacturing machinery and test equipment for computer components.

Prof. Sharon received his M.S. and Ph.D. in Mechanical Engineering from the Massachusetts Institute of Technology, and his B.S. in Mechanical Engineering from the Polytechnic Institute of New York. He is the Editor-in-Chief of the International Journal, *Robotics and Computer Integrated Manufacturing.*

In September of 2000, Prof. Sharon founded kSARIA Corporation, a well funded early-stage company focused on providing cutting-edge process automation equipment to the optical communication industry. Recently, he co-founded Boston Array Technologies, a company which develops new diagnostic tools based on peptide arrays synthesis technology.

Prior Professional Experience:

MIT Manufacturing Institute — **Cambridge, MA**
Co-founder and Executive Officer — 1991-1998

Co-founded the MIT Manufacturing Institute: an advanced technology development organization, established with seed funding from the National Science Foundation, to accelerate the process of scaling up basic research into usable technologies, processes and machinery for industry.

Worked closely with industry to develop automated machinery for optoelectronics and semiconductor manufacture, composites fabrication, medical applications, paper handling and high-speed assembly.

Led a large-scale effort aimed at reducing the manufacturing cost of optoelectronics and fiber optic systems through the development of cost-effective packaging and handling machinery. Developed and deployed automated machines for pigtailing fibers to chips, winding complex gyroscope coil patterns, assembling optical circuits and preparing fibers for attachment.

MIT Laboratory for Manufacturing and Productivity — **Cambridge, MA**
Associate Director — 1989-1991

Conducted research in the areas of cost-effective flexible automation, real time sensors, high-reliability transfer lines and composites fabrication.

Served as industrial liaison for the Laboratory.

IBM T.J. Watson Research Center — **Yorktown Heights, N.Y.**
1984-1989

Developed the first PC-based, computer-controlled industrial robot and worked on the automation of internal operations for the manufacture of computer components.

Conducted numerous public relations tours, demonstrations and talks on manufacturing automation.

IBM General Technology Division — **East Fishkill, N.Y.**
1981-1984

Worked on thermal packaging of multi-chip modules.
Designed test equipment for the life span of high-end computer modules.
Developed and implemented manufacturing processes for new computer modules.
Evaluated the impact of new product introductions on existing manufacturing lines.

U.S. Citizen

Publications of Dr. Andre Sharon

1. A. Sharon and D. E. Hardt, "Enhancement of Robot Accuracy Using Endpoint Feedback and a Macro-Micro Manipulator System," *Proceedings of the American Control Conference,* June 1984.

2. A. Sharon and E. Carey, "Real Time Control of an Anthropomorphic Robot Using AML and the IBM Personal Computer," *IBM Research Report (RC 11065 #49703),* March 1985.

3. A. Sharon and E. Carey, "AML + PC = CIM?" *Computers in Mechanical Engineering,* July 1985.

4. A. Sharon, "Pneumatically Servoed Robot Gripper," *IBM Research Report (RC 1134951140),* September 1985.

5. A. Sharon and D. E. Hardt, "More Analysis and Experimentation on a Macro / Micro Manipulator System," *Proceedings of the ASME Winter Annual Meeting,* December 1987.

6. A. Sharon, "High Bandwidth Force Regulation and Inertia Reduction Using a Macro / Micro Manipulator System," *Proceedings of the IEEE International Conference on Robotics and Automation,* April 1988.

7. A. Sharon, N. Hogan, and D. E. Hardt "Controller Design in the Physical Domain (Application to Robot Impedance Control)," *Proceedings of the IEEE International Conference on Robotics and Automation,* May 1989.

8. A. Sharon, N. Hogan, and D. E. Hardt, "Controller Design in the Physical Domain," *Proceedings of the American Control Conference,* June 1989.

9. A. Sharon, Ed. *Issues in Design/Manufacture Integration – 1990,* ASME Publication #G00542, New York, November 1990.

10. A. Sharon, N. Hogan, and D. E. Hardt, "Controller Design in the Physical Domain," *Journal of the Franklin Institute,* Volume 328, No. 5/6 pp. 697-721, 1991.

11. A. Sharon, Ed. *Issues in Design/Manufacture Integration – 1991,* ASME Publication #H00708, New York, November 1991.

12. N. Hogan, H.I. Krebs, J. Charnarrong, P. Srikrishna, and A. Sharon, "MIT-MANUS: A workstation for Manual Therapy and Training I," *Proceedings of robot and Human Communication RO-MAN '92 – IEEE,* Tokyo, September 1992.

13. N. Hogan, H.I. Krebs, J. Charnarrong, P. Srikrishna, and A. Sharon, "MIT-MANUS: A Workstation for Manual Therapy and Training II," *Proceeding of the SPIE (Society of Photo-optical Instrumentation Engineers) Conference on Telemanipulator Technology,* Boston, November 1992.

14. A. Sharon, N. Hogan, and D.E. Hardt, "The Macro / Micro Manipulator: An Improved Architecture for Robot Control," International *Journal of Robotics and Computer Integrated Manufacturing,* Volume 10, No. 3, pp. 209-222, June 1993.

15. V. Sharma and A. Sharon, "Optimal Orientation of Flakes in Oriented Strand Board (OSB)," *Journal of Experimental Mechanics,* Volume 33, No. 2, pp. 91-98, June 1993.

16. A. Sharon, "Fostering Technology Transfer Through Industry-University Cooperation: A Practitioner's View at MIT," *Empirica,* Volume 21, No. 3, pp. 285-296, 1994.

17. A. Sharon and S. Lin, "Development of an Automated Fiber Optic Winding Machine for Gyroscope Production," *International Journal of Robotics and Computer Integrated Manufacturing*, Volume 17, No. 3, pp. 223-231, June 2001.

18. A. Sharon, A. Bilsing, G. Lewis, and X. Zhang, "Manufacturing of 3D Microstructures Using Novel UPSAMS Process for MEMS Applications," Nano and Microelectromechanical Systems (NEMS and MEMS) and Molecular Machines, *Proceedings of the Materials Research Society Syposium*, 2003

19. A. Sharon, A. Bilsing, G. Lewis, and X. Zhang, "Manufacturing of 3D Microstructures Using Novel UPSAMS Process (Ultra Precision Manufacturing of Self-Assebled Micro Systems)," *Proceedings of the IEEE 16th International Conference on Micro Electro Mechanical Systems (MEMS 03)*, Kyoto, Japan, January 2003.

I hereby certify that a true copy of the Expert Report of Andre Sharon, Ph.D. was served upon the attorneys of record for plaintiff Vision BioSystems (USA) Trading, Inc. by overnight courier on June 8, 2004:

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EXHIBIT

E

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

VISION BIOSYSTEMS (USA) TRADING, INC., Plaintiff, v. VENTANA MEDICAL SYSTEMS, INC., Defendant.	CIVIL ACTION NO. 03-CV-10391-GAO

EXPERT REPORT OF DAVID G. HICKS, M.D.

1. I am the Director of the Section of Surgical Pathology, and Co-Director of the Morphologic Molecular Pathology Laboratory, at the Cleveland Clinic Foundation. Previously, I was an Associate Professor in the Department of Pathology and Laboratory Medicine, with a joint appointment at the Cancer Center, at the University of Rochester School of Medicine, and an Attending Physician at the University of Rochester Medical Center.

2. I received a Bachelors of Arts degree from Canisius College of Buffalo, New York, and a Doctor of Medicine degree from the University of Rochester School of Medicine and Dentistry. A copy of my resume is attached as Exhibit A.

3. I serve on the editorial board of the Journal of Bone and Joint Surgery, and previously served on the editorial board of the International Journal of Surgical Pathology. I also serve as an ad hoc reviewer for the Journal of Cancer and the American Journal of Pathology. I am a member of the United States and Canadian Academy of Pathology, the College of

Pathology, and the Eastern Cooperative Oncology Group. I am a Diplomat of the American Board of Pathology, and am licensed to practice medicine in Pennsylvania, New York, and Ohio.

4. I have been retained by the firm of Wilson Sonsini Goodrich & Rosati as a consultant in connection with the above-captioned lawsuit. For my work on this matter, I am being compensated at my consulting rate of $350 per hour. I have not testified as an expert at trial or by deposition within the preceding four years.

5. If called as an expert witness in this matter, I anticipate that my testimony may concern the matters addressed below. My anticipated testimony may be affected by the production of additional information and/or positions plaintiff takes on the topics set forth in this report. I have been informed that plaintiff may communicate at least some of those positions to defendant some time after this report is prepared, such as in the form of deposition testimony to be given by its experts. After I have an opportunity to review those materials, I may amend this report.

6. In connection with formulating the opinions set forth in this report, I have reviewed at least the following material: U.S. Patent No. 6,352,861 ("the '861 patent") and portions of its prosecution history; Expert Report of Doug Koebler Regarding U.S. Patent No. 6,352,861 ("the Koebler Report"), and the materials attached to that report; Keenan et al., *Patient Identification in an Automated Clinical Laboratory System*, IEEE Frontiers of Eng. in Health Care, 15-18 (1982) ("Keenan"); Tilzer et al., *Use of Bar Code Labels on Collection Tubes for Specimen Management in the Clinical Laboratory*, Arch. Pathol. Lab. Med., 112:1200-1202 (Dec. 1988) ("Tilzer"); Hauser, *Specimen Holder*, U.S. Patent No. 4,159,875 (1979) ("Hauser"); English translations of Kojima et al., *Analyzing Method of Blood Image*, Japanese Pat. App. Pub. No. 55-107957 (1980) ("JP '957"); Liston, *Automated Analysis Instrument System*, U.S. Patent

No. 4,528,159 (1985) ("Liston"); Driscoll et al., *Discrete Automated Chemistry System with Tableted Reagents*, Clin. Chem., 29:1609-1615 (1983) ("Driscoll"); and English translations of Japanese Pat. App. Pub. No. 63-61165 (1988) ("JP '165").

7. In paragraph 17 of his report, Mr. Koebler describes a person of ordinary skill in the art. This description fails to appreciate the applications to which the '861 patent is applied in the field of diagnostic pathology. The person having ordinary skill in the art to which the '861 patent pertains would have knowledge of, or would consult a diagnostic pathologist with experience in, how tissues samples on slides are processed and treated in the pathology laboratory and the role of the pathologist in evaluating tissue samples and arriving at an accurate assessment.

8. In paragraphs 39-40 of the Koebler Report, Mr. Koebler suggests that it would have been obvious to use the instrument described in Liston and Driscoll for automating the complex protocols in slide staining. This fails to take into account the perspective of the pathologist, who must examine the tissue, select the most appropriate staining protocol, and examine the product of the slide staining process to make an accurate determination based on the staining reaction in the context of the morphologic appearance of the sample.

9. JP '957, Liston, and Driscoll disclose fundamentally different applications from that which is used in connection with the '861 patent. The '861 patent contemplates the application of reagents to slide-mounted tissue samples. Those samples are typically obtained by an invasive procedure in order to make a determination of whether a disease is present and of what type. The samples must be handled in a careful and delicate manner, and the procedures applied to the samples are highly individualized.

10. By contrast, JP '957 concerns routine staining of blood smears for laboratory analysis. This staining is performed to visualize blood cells under the microscope, and typically the same staining protocol is applied to every patient regardless of the clinical context. The bar code on the slide in JP '957 is linked to information about the container holding the blood sample, but does not have anything to do with the actual slide staining. In fact, the exact same staining protocol will be applied to different bar coded slides in a cassette, and the bar code on the slide plays no role in determining the nature of the staining to be performed. Thus, JP '957 does not address the individualized treatment, and the complexity and subjectivity of the analysis, of each different tissue sample with which a pathologist would be concerned. By contrast, the '861 patent allows bar coding to determine customized staining protocols on each slide, in accordance with the impressions and needs of the pathologist.

11. Liston and Driscoll describe systems for making analytic chemistry measurements on patient blood samples. The samples are provided in standard test tubes, which may be bar coded. The systems transfer the patient blood samples from the test tubes to cuvettes, where chemical reactions take place. The cuvettes also receive reagent tablets, which may be broken up and dissolved with the aid of an ultrasonic device. This approach is antithetical to the handling and analysis of samples in the diagnostic pathology laboratory. First, the blood samples processed by the Liston and Driscoll systems are obtained in a fairly routine manner in comparatively large volumes. An automated system where samples and reagent tablets are combined in cuvettes is much simpler to implement, as compared to the diagnostic pathology context. Tissue samples used with the '861 patent are typically obtained by an invasive procedure, are delicate and need to be handled carefully, and may be irreplaceable. Decisions about the need to apply a specific slide staining protocol are only considered after an initial

morphologic assessment of the H&E stained section by the pathologist. Therefore, given the different nature of the tissue sampling and handing requirements, it would not have been obvious to apply the systems of Liston and Driscoll to pathological tissue samples. Second, analytic chemistry tests typically generate a quantitative measurement of an analyte, which can be conducive to automation. By contrast, performing staining protocols and interpreting stained tissue samples requires a much more subjective and individualized interpretation of tissue morphology, which by its very nature is less intuitively susceptible to automation.

12. For the above reasons, I disagree with the implication in paragraph 40 of the Koebler Report that a slide is comparable to the sample containers described in Liston and Driscoll.

13. In paragraph 41 of the Koebler Report, Mr. Koebler relies on two citations from Tilzer and suggests that automated bar code systems can be equally applied to all medical applications. This is a gross overgeneralization and does not apply to the intended pathology laboratory users of the '861 patent. The analysis and interpretation of tissue slide samples in the pathology laboratory is very different than the applications of automated bar coding described by Tilzer. The applications identified by Tilzer concern the use of bar codes to track particular items in the hospital, but bar codes are not used with an individualized approach such as is done with the '861 patent. In fact, Tilzer is conspicuous in its failure to identify the diagnostic pathology laboratory in its list of potential applications for bar codes. This further confirms that, in the late 1980's, automated bar code systems were not contemplated as able to perform complex staining reactions on tissue sections, such as described by the '861 patent. The Koebler Report points to nothing in the prior art or knowledge in 1990 that suggests combining JP '957, Liston, and Driscoll in a manner to obtain claims 1, 2, 3, 5, 6 and 8 of the '861 patent.

14. Prior to the introduction of Ventana's automated slide staining systems, with functionality as described in claims 1, 2, 3, 5, 6 and 8, advanced tissue staining procedures such as immunohistochemistry were performed manually, largely in sophisticated university laboratories. Because slide staining protocols involved complex labor intensive techniques that required considerable experience and judgment, automation of these steps was initially met with skepticism by the pathology community.

15. Ventana's automated slide staining systems, with functionality as described in claims 1, 2, 3, 5, 6 and 8, came to be recognized by the pathology community as providing a significant advance in tissue sample analysis. The automation of the Ventana systems provided a number of advantages, including a level of consistency and reliability that was not achievable with manual processing. It also substantially improved laboratory capacity and turn-around time for completing the applicable staining protocols.

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Awards, Honors and Fellowships:

1981-82	Medical Student Fellowship, Department of Pathology, University of Rochester, Rochester, New York
1984	Member, Alpha Omega Alpha Honor Medical Society
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1989	Stowell-Orbison Award, United States and Canadian Academy of Pathology

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1995	Kappa Delta Elizabeth Winston Lanier Award for Outstanding Orthopaedic Research, American Academy of Orthopaedic Surgeons
1996	Andrew W. Mellon Dean's Teaching Scholar, 1996-1999
1997	Duthie-Evarts Resident Education Award presented by the Department of Orthopaedics
2002	John Beach Hazard Distinguished Teaching Award, presented by Cleveland Clinic Foundation, Department of Pathology and Laboratory Medicine.

Postgraduate Training:

1984-85	Intern, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia PA
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1984-85	Assistant Instructor, Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia Pennsylvania
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Hospital Appointments:

1989-1990	Attending Staff, Hospital of the University of Pennsylvania, Philadelphia PA
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Membership in Professional and Scientific Societies:
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American Society for Bone and Mineral Research

Editorial Boards:
International Journal of Surgical Pathology, Editorial Board
Journal of Bone and Joint Surgery, Editorial Board

Cancer, Ad Hoc reviewer
American Journal of Pathology, Ad Hoc reviewer

GRANT SUPPORT:

National Institutes of Health, AR 40325. Autocrine and Ionic Regulation of Chondrocyte Phenotype. 5/92-4/96. R.N. Rosier, PI, D.G. Hicks, co-I; $144,537/year

Bristol Meyers SquibblZimmer, Orthopaedic Research and Education Foundation Institutional Award. Molecular Pathology in Orthopaedics. 7/91-6/96. R.N. Rosier, PI, D.G. Hicks, co-I, J.E. Puzas, co-I; $50,000/year

Oral and Maxillofacial Surgery Foundation. Correlation of Magnetic Resonance Images of the Bone Marrow of the Mandibular Condyle with Histologic Observations in Core Biopsies Obtained in Patients Undergoing TMJ Surgery. 3/92-3/94. P.L. Westesson, PI, D.G. Hicks, co-I; $35,000 .

National Institutes of Health, BRSG, PHS57RR05403-30. Growth factor and matrix protein expression in skeletal neoplasms. 7/91-6/92. D.G. Hicks, PI; $4,500/year

Arthroscopy Association of North America. Chondrogenesis and osteogenesis in arthrofibrotic tissues of the knee. 4/92-3/93. W.J. Sebastianelli, PI, D.G. Hicks, co-I; $14,440/year

Eastman Dental Center. In vitro and in vivo principles of site directed bone formation. 7/92-6/93. J.E.Puzas, PI. D.G. Hicks, co-I; $10,000/year

DePuy Inc. In vitro and in vivo principles of site directed bone formation. 5/92-4/94. J.E. Puzas, PI. D.G. Hicks, co-I; $55,000/year

Buswell Fellowship. 7/93-6/94. Awarded to DG Hicks; $10,000

National Institutes of Health, R29ES07138-01. Effects of lead on the epiphyseal growth plate. 7/95-11/00. D.G. Hicks, PI. $70,000/year

National Institutes of Health. CA 71603-0 I. Growth plate radiation response: mechanisms and therapy. 4/97-3/01. R.N. Ro~ter, PI. D.G. Hicks, co-I; $156,815/year.

National Institutes of Health, ES08121-O1. The effect of lead on skeletal remodeling in vitro. 4/97-3/01. J.E. Puzas, PI. D.G. Hicks, co-I; $144,941/year

Current Administrative Responsibilities

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TEACHING CONTRIBUTIONS

* University of Rochester, School of Medicine Pathology Courses, second year class;
General Pathology Course, second year class; Laboratory instructor, Fall 1990-1994
Musculoskeletal system- Lectures on the pathology of bone tumors, the pathology of soft tissue tumors, normal joint function and physiology, and the pathology of arthritis.
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Lymphoreticular system, Laboratory instructor, Spring 1991-2001

* Orthopaedic Pathology Elective

* Advisor for medical student and pathology residents research projects

* Weekly pathology teaching conference for Orthopaedic Surgery Residents, 1990-1999

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PUBLICATIONS

Original Papers:

1. Bhandari AK. Nanda NC. **Hicks DG**: Two-dimensional echocardiography of intracardiac masses: Echo pattern-histopathology correlation. Ultrasound in Med Bioi. 8(6):673-680, 1982.

2. Perry IC. Nanda NC, **Hicks DG**. Harris IP: Two-dimensional echocardiographic identification of aortico-left ventricular tunnel. Am J Cardiology, 52:913-914. 1983.

3. Taves DR. Forbes N. Silverman D. **Hicks DG**: Inorganic fluoride concentrations in human and animal tissues. In: Fluorides: Effects on Vegetation. Animals and Humans. I.S. Shupe, H.B. Peterson. and N.C. Leon (eds.). Paragon Press. Inc., Salt Lake City, Utah, 1983.

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Chiesa-Vottero AG, Castilla EA, Borden E, Hartke M, **Hicks DG**, Tubbs RR, Goldblum JR. Epidermal growth factor receptor (MPNST): An immunohistochemical and fluorescence in-situ hybridization (FISH) analysis. Mod Pathol 16:29A; 2003. (poster presentation at the Annual Meeting of the United States and Canadian Academy of Pathology, March 2003).

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Shao YY, Wang L, **Hicks DG**, and Ballock RT. Using Laser Capture Microdissection to examine gene expression in functionally distinct populations of growth plate chondrocytes. (Poster presentation, American Society for Bone and Mineral Research, annual meeting, 2003).

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Tubbs R , Skacel M, Pettay J, Powell R, Mele J, Downs-Kelly E, **Hicks D**, Hainfeld J. Enzyme metallography (EnzMet): A novel second-generation bright field assay for detection of HER2 gene amplification in breast carcinoma. Poster Presentation Association for Molecular Pathology 2003

Willis-Eppinger G, His E, **Hicks DG**. Automated instrumentation in immunohistochemistry (IHC): improvements in efficiency and turnaround time. (Poster presentation for the National Society of Histotechnology annual meeting, 2003).

Safran O, Derwin KA, Powell K, Ilaslan H, **Hicks DG**, Iannotti JP. Rotator cuff muscle atrophy and passive tissue tension after chronic detachment in a canine model. (Platform presentation, Orthopaedic Research Society annual meeting, 2003).

D. Hicks, M. Skacel, E. Downs-Kelly, M. Cheang, J. Pettay, T. Nielsen, D. Huntsman, R. Powell, J. Hainfield, T. Grogan: Invasive breast cancer clinical outcome is predicted by a novel bright-field assay for the simultaneous detection of HER2 gene amplification and protein

expression (SILVERFISH). Submitted American Society of Clinical Oncology Annual Meeting 2004

G.T. Budd, E. Tso, B. Yoder, T. Choueiri, P. Elson, S. Tarr, M. Skacel, R. Tubbs, A. Dawson, **D. Hicks**; Using novel protein antibodies on tissue microarrays (TMAs) for breast cancer prognostication. American Society of Clinical Oncology Abstract Submission 2004

Skacel M, Tubbs R, Pettay J, Powell R, Mele J, Downs-Kelly E, **Hicks D**, Hainfield J. Enzyme Metallography (ENZMET): A Novel Second-Generation Bright Field Assay for Detection of HER2 Gene Amplification in Breast Carcinoma. Poster Presentation Association for Molecular Pathology 2003

D G Hicks, A G Chiesa, E Borden, M Hartke, R R Tubbs, S Tarr, J R Goldblum. Epidermal Growth Factor Receptor (EGFR) expression in Synovial Sarcoma (SS): An immunohistochemical (IHC), Fluorescence In Situ Hybridization (FISH), and Quantitative image analysis study. Accepted for poster presentation United States and Canadian Academy of Pathology Annual Meeting 2004

B J Yoder, E Tso, M Skacel, T Choueiri, S Tarr, T Budd, R R Tubbs, J Adams, A E Dawson and **D G Hicks**. The Expression of Fascin, an Actin Bundling Motility-Associated Protein in Breast Cancer. Accepted for poster presentation United States and Canadian Academy of Pathology Annual Meeting 2004

E Downs-Kelly, M Stoler, R Tubbs, M Skacel, T Grogan and **D Hicks**. The Influence of Polysomy 17 (CEP17+) on HER2 Protein Expression in Carcinoma of the Breast. Accepted for poster presentation United States and Canadian Academy of Pathology Annual Meeting 2004

J Fine, E Downs-Kelly, **D Hicks**, J Pettay, S Tarr, T Ruddy R Powell, J Mele, J Hainfield, T Grogan, M Skacel, D Borthwick, and R Tubbs. High-throughput image analysis of HER2 gene amplification detected by second-generation gold-facilitated autometallographic bright field *in-situ* hybridization assay (GOLDFISH). Accepted for poster presentation United States and Canadian Academy of Pathology Annual Meeting 2004

D Hicks, M Skacel, E Downs-Kelly, M Cheang, J Pettay, F D Hsu, T O Nielson, J Mele, D G Huntsman, R Powell, J Hainfeld, T Grogan and R Tubbs. SILVERFISH-A Novel Bright Field Assay for Simultaneous Detection of HER2 Gene Amplification and Protein Expression Predicts Clinical Outcome in Invasive Breast Cancer. Accepted for poster presentation United States and Canadian Academy of Pathology Annual Meeting 2004

R Tubbs, J Pettay, M Skacel, E Downs-Kelly, **D Hicks**, R Powell, P Roche, T Grogan, J Mele and J Hainfeld. Analytical Validation of SILVERFISH, a Bright Field Second Generation Autometallographic Assay for Concomitant Detection of HER2 Gene Amplification and Encoded Protein Expression. Accepted for poster presentation United States and Canadian Academy of Pathology Annual Meeting 2004

D G Hicks, M Skacel, G T Budd, M Hartke, J Pettay, and R R Tubbs. Incidence of Topoisomerase II-alpha (TOP2A) Co-amplification and Deletion of Adenocarcinoma of the Breast with HER2 Gene Amplification. Accepted for poster presentation United States and Canadian Academy of Pathology Annual Meeting 2004

NATIONAL WORKSHOPS AND INVITED PRESENTATIONS:

Faculty: *Orthopedic Pathology Review Course.*
Harry Schwamm, M.D., Course Director, Atlantic City, NJ. Newport Beach. CA. and Philadelphia. P A. 1989-1996. (Sponsored by the Departments of Pathology and Orthopaedics, The Graduate Hospital. Philadelphia. PA).

Faculty: Workshop on: In situ Hybridization: Non-radioactive in situ hybridization using digoxigenin labeled oligonucleotide probes: application to musculoskeletal tissues. Presented at the *New York State Histotechnological Society Annual Meeting and Seminar.* Buffalo. NY, April 1993.

Guest faculty: Symposium on: Diagnosis and management of musculoskeletal neoplasms. Harry Schwamm, M.D.. Course Director. Philadelphia PA, April 1993 (Sponsored by the Departments of Pathology and Orthopaedics, The Graduate Hospital. Philadelphia. PA).

Guest speaker: The effects of lead on bone structure and function. Presented at the *Workshop on Skeletal Lead.* NIEHS, Research Triangle Park, NC, September 27-28, 1993. (Sponsored by the National Institute of Environmental Health Sciences and the Carnegie Foundation).

Faculty: Workshop on: Non-decalcified plastic embedded sectioning of skeletal tissue in the evaluation of metabolic bone disease and other skeletal disorders: clinical, biologic, and technical considerations. Presented at the *New York State Histotechnological Society Annual Meeting and Seminar*, Albany, NY, April 1994.

Guest speaker: Non-neoplastic diseases of the skeleton: Metabolic bone disease and osteoporosis, fractures, and osteomyelitis. Millard Fillmore Health System, Department of Pathology, C.M.E meeting, October 10, 1995.

Guest speaker: The interaction of tumor cells with the bone environment: lessons from small round blue cells. Presentation to the Western New York Society of Pathologists, Buffalo, NY January 24, 1996.

Guest speaker: The role of the bone biopsy in the evaluation of osteoporosis. *Osteoporosis for the primary care physician.* Rochester Academy of Medicine, Rochester, NY, April 19, 1996.

Faculty: Workshop on: Cytopathology of bone and soft tissue lesions: An integrated approach to differential diagnosis. *American Society of Clinical Pathologists Fall Meeting,*

San Diego, CA, October 2, 1996.

Co-Director: Workshop on: Nonradioactive in situ hybridization using oligonucleotide probes: Research and clinical applications, *National Society for Histotechnology Annual Meeting,* Albuquerque, NM, October 21, 1996.

Invited lecture: "Pathology, new technologies, new directions, the next 75 years: The role of anatomic pathology in the rapidly expanding area of molecular and nucleic acid therapeutics. Address to the *Advisory Council, American Society of Clinical Pathologists, Spring Meeting*, Chicago, IL, April 6, 1997.

Faculty: Workshop on: Cytopathology of bone and soft tissue lesions: An integrated approach to differential diagnosis. *American Society of Cytopathology 45th Annual Meeting*, Boston, MA, November 8, 1997.

Invited lecture: "Cytopathology of bone: An integrated approach to differential diagnosis." Western New York Society of Pathologists, Buffalo, New York, November 19, 1997.

Invited lecture: "The Pathology of Joint Disease." Department of Pathology, State University of New York at Buffalo, Buffalo General Hospital, Buffalo, New York, November 19, 1997.

Guest speaker: What is the value of a bone biopsy in the evaluation of a patient with osteoporosis? : *Basic and Advanced Principles in the care of the osteoporotic patient*. Marriott-Airport Hotel, Rochester, NY, April18, 1998, Sponsored by the University of Rochester School of Medicine and Dentistry Office of Continuing Professional Education.

Guest speaker: Skeletal pigmentation as a result of medications and metabolic diseases. Cleveland Society of Pathology. February, 2002.

Guest speaker: Automated In-situ Hybridization and Gene Expression Profiling: An Update. Society for Applied Immunohistochemistry, Quarterly Meeting, Memorial Sloan-Kettering Cancer Center, New York, New York, July 17, 2002.

Guest speaker: Automated In-situ Hybridization: A tool for gene discovery. International Society for Analytical and Molecular Morphology, Annual Meeting, Santa Fe New Mexico, September 15-19, 2002.

Faculty, workshop presentation: Immunohistochemistry and the critical evaluation of controls. Presented at the 28th annual National Society for Histotechnology Symposium, Long Beach, California, September 28- October 3, 2002.

Invited seminar speaker: The molecular mechanisms of skeletal metastatic disease and the disruption of normal bone remodeling. Genentech BioOncology, San Francisco California, October 16th, 2002.

Participant, Pathology Advisory Board Meeting for, Genentech BioOncology, the Claremont Resort, Berkeley, California, October 16-18, 2002.

Invited seminar speaker: Prognostic markers in breast cancer management. As part of, Molecular Diagnosis in Women's Health; an Educational Forum. New England Medical Center, Boston Mass, October 22, 2002.

Invited seminar speaker: Prognostic markers in breast cancer management. As part of, Molecular Diagnosis in Women's Health; an Educational Forum. Stanford University Medical Center, Palo Alto California , November 1, 2002.

Invited seminar speaker: Prognostic markers in breast cancer management. As part of, Molecular Diagnosis in Women's Health; an Educational Forum for Pathologists, Magee Women's Hospital of UPMC Health System, Pittsburgh PA, January 2003.

Invited seminar speaker: Prognostic markers in the evaluation of breast cancer: The role of the pathologist. Eastern Great Lakes Pathology, X-Cell Laboratories of Western New York, Buffalo New York, March 2003.

Invited Presentator: Pathology Grand Rounds. Molecular Mechanisms Mediating Metastasis to the Musculoskeletal system. University Hospitals of Cleveland, Institute of Pathology, Cleveland OH, March 2003.

Moderator: Platform session, Bone and soft tissue. Annual Meeting of the United States and Canadian Academy of Pathology, March 2003.

Invited seminar speaker: Tissue based studies of gene expression: The utility of automated ISH and TMA's in gene discovery and clinical validation. University of Minnesota, Cytogenetics, Molecular Diagnostics, Lab Med, and Surgical Pathology. Minneapolis MN, April 2003.

Workshop: Resident Review Course. Bone Pathology: An integrated approach to diagnosis. American Society for Clinical Pathology, Hoffman Estates, Chicago IL, April 2003.

I hereby certify that a true copy of the Expert Report of David G. Hicks, M.D. was served upon the attorneys of record for plaintiff Vision BioSystems (USA) Trading, Inc. by overnight courier on June 8, 2004:

Elizabeth A. Leff, Esquire
Rothwell, Figg, Ernst & Manbeck
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24 School Street
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Roger J. Chin

EXHIBIT F

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

VISION BIOSYSTEMS (USA) TRADING INC. Plaintiff, v. VENTANA MEDICAL SYSTEMS, INC. Defendant.	Civil Action No. 03 CV 10391 GAO

SUPPLEMENTAL EXPERT REPORT OF DOUG KOEBLER REGARDING U.S. PATENT NO. 6,352,861

1. The purpose of this supplemental report is to discuss additional prior art references that I have reviewed since I submitted my report dated April 8, 2004 ("Original Report"). I have also reviewed the reports of Dr. Sharon and Dr. Hicks since submitting my original report. While I disagree with many statements made in those reports, I do not discuss these in this supplemental report. To the extent that I was asked, many of these disagreements were addressed during my deposition taken on July 2, 2004.

2. My background and qualifications are set forth in my Original Report. A list of the additional references I reviewed in preparing this supplemental report is attached as Exhibit A.

3. In my Original Report, I analyzed claims 1, 2, 3, 5, 6, and 8 of the '861 patent ("the asserted claims") using the interpretation advocated by Ventana that they cover the Bond instrument. I understand that the Court has now interpreted these claims and determined that these claims cover the Bond instrument. The Court's claim interpretation, therefore, does not change the analysis set forth in my Original Report. The additional analysis set forth in this supplemental report is based on the Court's interpretation that the asserted claims are infringed by the Bond instrument.

4. The additional prior art references that I have reviewed since I submitted

my Original Report include the following:

a. U.S. Patent Number 4,430,299 to Horne, "Apparatus for Monitoring Chemical Reactions," filed June 18, 1981, issued on February 7, 1984 (Horne '299). This patent describes a computer-controlled chemical analyzer that uses bar-coded sample slides. The sample is placed on the slide outside the instrument. Reaction reagents are already on the slide at the time the sample is applied. Horne '299, col. 6, lines 32-52, Col. 8, lines 45-48. The slides are then inserted into slots in the instrument cover. Id., col. 4, lines 8-11. A slide bar code serves two functions: it identifies the patient sample and includes test instructions. Id., col. 6, lines 58-61, col. 8, lines 51-54. The instrument includes a reader for reading the bar code. Id., col. 7, lines 42-48. The instructions encoded by the bar code can include information that the computer uses to control reaction parameters, such as the temperature of a particular heater during a particular test. Id., col. 9, lines 14-20. The bar code also can encode instructions to the computer concerning the timing of tests. Id., col. 5, lines 33-36, col. 9, lines 4-11. The slide bar codes allow random access of slides – specific positioning is avoided. "Any cartridge [i.e., slide] may be inserted or removed at will without disturbing any of the other cartridges and without stopping rotation of the rotor." Id., col. 4, lines 11-13. Horne '299 states that he refers to slides generically as "sample support members" because in his apparatus, a slide "serves the same purpose as a cuvette" in the prior art instruments he described in his patent. Id., col. 5, lines 64-68.

b. Rappoport, Arthur, E., "If Bar Codes Work in Supermarkets, It Should Be Great for Medicine," Pathologist, February 1985. ("Rappoport") Dr. Rappoport, in an article published in a journal directed to pathologists, states that bar codes can be used to identify laboratory and blood bank patient specimens and that bar codes can be used by pathologists for more efficient and modern laboratory management.

c. Advertisement: "The Age Of Easy Diagnostic Testing," EM Diagnostic Systems, Inc., as published in Clinical Chemistry, Vol. 31, No. 6, 1985 ("Easy Diagnostic"). This advertisement describes a random access system

in which "cuvette bar codes automatically program all instrument parameters including test selection, sample/diluent selection and addition, wavelength, preincubation, and reaction times." The operator selects the tests to perform simply by selecting the appropriate bar-coded cuvette. The advertisement states that the "Analyzer and bar-coded cuvettes allow walk-away operation resulting in significant time savings and increased productivity."

d. Advertisement: Abbott Spectrum, as published in Clinical Chemistry, Vol. 3, No. 31, 1985 ("Spectrum"). This advertisement describes an instrument in which "on-board reagents are barcoded for automatic identification . . . ."

e. Advertisement: "Parallel Analytical System," American Monitoring Corporation, as published in Clinical Chemistry, Vol. 31, No. 1, 1985, p. 20A ("Parallel"). This advertisement shows a chemical analyzer which uses a bar code on a sample container in which the schedule of tests and patient identification are encoded.

f. U.S. Patent No. 4,800,762 to Sugaya, "Liquid Depositing Device," filed June 16, 1987, issued January 31, 1989 ("Sugaya '762 "). This patent describes a device for automatically depositing a desired amount of sample liquid on the reagent layer of a chemical assay slide. Sugaya '762, col. 2, lines 53-59. A suction-and-discharge mechanism includes a piston that is slidable within a fluid passage and is actuated by a pulse motor to draw liquid sample into and dispense liquid sample from a depositing tip. Id., col. 3, lines 20-37. The amount of liquid drawn from a sample container and thereafter deposited onto the assay slide is controlled by the amount of travel of the piston. Id., col. 3, line 68 - col. 4, line 4. A controller controls the pulse motor via control signals, thereby controlling the quantity of sample drawn into and deposited from the depositing tip. Id., col. 4, lines 21-28. Since the desired quantity of sample deposited on the assay slide depends on the type of slide, "it is preferred that the quantity of the sample liquid be automatically determined by the chemical assay system by reading a bar code or the like provided on the assay slide 5 to indicate the quantity

of the sample liquid to be deposited on the specific slide. . . ." Id., col. 4, lines 33-41.

5. As demonstrated in my Original Report, all elements of the disputed claims are described by the combination of Liston/Driscoll and JP '957. In that report, I also explained why I believe that it would have been obvious to a person of ordinary skill in the art to combine those teachings. The additional references discussed above, as well as the admitted state of the art as reflected by the prior art discussed in the '861 patent, also disclose elements of the disputed claims and further support my view that it would have been obvious to combine the teachings of Liston/Driscoll and JP '957.

6. The background art described in the '861 patent shows that at the time of filing, computer-controlled processes for dispensing reagents onto slides were known in the art. The '861 inventors acknowledge in the "Background Section" of the '861 patent that "[a]utomated systems have been explored to introduce cost savings, uniformity of slide preparations, and reduction of procedural human errors." '861 patent, col. 1, lines 53-55. They explain that, for example, the Stark article describes a microprocessor controlled system that delivers a predetermined volume of liquid to a slide from each syringe. Id., col. 1, line 65 - col. 2, line 5. The inventors further explain that the Cosgrove article "describes an immunostaining apparatus for auto-pipetting reagents into a slide well from a carousel holding up to 18 reagent vials." Id., col. 2, lines 6-9.

7. While the Liston/Driscoll and Tilzer references do not explicitly describe a configuration of their systems in which a sample container also serves as a reaction vessel, such use would be implicit to a person skilled in the art. I know from my experience and training that sample containers can be, and often are, used as reaction containers. As described, for example, in Horne '299 and Easy Diagnostic, it was known prior to the '861 filing date that a bar code identifying a sample and/or test procedures could be placed directly on the reaction vessel. The relevance of Liston is not in whether the sample tube could also function as a reaction vessel. The primary relevance of Liston to my analysis is that it teaches that in an automated analyzer instrument, bar codes can be used on randomly-placed sample carriers, the bar code can be read by the instrument, and the information contained in the bar code can be used by the instrument controller to

identify the sample and determine the test(s) to perform (e.g., the reagents to dispense) on the sample. Moreover, the system described in the Liston/Driscoll references uses cuvettes as the reaction vessels because of the particular detection/quantification methodology employed (spectrophotometric analysis, i.e., light transmission), and, importantly, so that multiple tests can be performed on a single sample by transferring aliquots from the sample container to multiple cuvettes. If these system goals were not important (e.g., as in the case of an automated slide staining system) it would have been quite obvious to apply a bar code to a vessel that serves both as the sample carrier and the reaction vessel. JP '957, Horne '299, and other prior art show that the vessel/carrier can be a slide.

8. Horne '299 teaches the use of bar codes on a sample-carrying reaction slide. The bar codes identify the sample and provide test instructions to the instrument. Liston/Driscoll and Easy Diagnostic describe instruments that dispense reagents, and Horne '299 describes an instrument in which the slide bar codes instruct the instrument regarding the procedure to be performed on the slide, including timing and heating instructions that are communicated to the instrument controller. These instructions, like the instructions for dispensing a particular reagent as disclosed in the '861 patent and in Liston/Driscoll, are simply instructions for controlling electro-mechanical devices (e.g., robotic pipetting devices, heater elements, etc.). Moreover, as discussed in paragraph 6 above, the '861 inventors acknowledged that computer-controlled instruments for dispensing reagents onto slides were known prior to the '861 filing date. These disclosures further confirm my opinion that it would have been obvious to use information carried in a slide bar code to control a device for dispensing reagents onto slides.

9. In Horne '299, test instructions can be encoded into the slide bar code. The computer can also be instructed to indicate when a particular test is completed so an operator can remove the completed slide. To be able to indicate when a particular test is done, the instrument needs to know where that slide is located. What this tells me as one of skill in the art is that the instrument reads the slide's bar code and communicates the test instructions and position of that slide to the instrument computer.

10. Horne '299 explains that a disadvantage of a prior art system overcome by the invention is that in the prior art system, even though a reaction end point has been reached for a particular sample, that sample will remain in the instrument until the turntable has completed a revolution, thereby wasting time while the completed sample sits on the turntable. Horne '299, col. 3, lines 30-41. Horne '299 explains that any cartridge (i.e., slide) may be inserted or removed at will without disturbing the other cartridges and without stopping the instrument. As one skilled in the art, this tells me that a sample slide can be randomly placed in the Horne '299 instrument and a particular test performed on that slide. The Horne '299 instrument is able to do this because the slide bar code identifies the sample and provides test instructions to the instrument computer.

11. Easy Diagnostic is another example of an instrument that uses bar codes on the reaction container (the Easy Test cuvette) to instruct the instrument what test procedure to perform on the sample. The bar code information includes instructions for "sample/diluent selection and addition."

12. The Abbott Spectrum advertisement is further evidence (along with Driscoll and JP '165, discussed in my Original Report) that using bar codes on reagent containers to allow the instrument to identify reagents was known prior to the '861 filing date.

13. The Parallel instrument is an example of an instrument that uses a bar code to identify a sample and to instruct the instrument on what procedures to perform on the sample.

14. Sugaya '762 describes a device that uses bar codes on the assay slides to provide information to the instrument controller to enable the controller to automatically determine the quantity of sample to be dispensed onto the slide. The controller then controls the dispensing apparatus to dispense the desired quantity of sample on the assay slide.

15. Instruments that use bar codes on sample or reaction containers to instruct the instrument's computer which test procedure to perform on the particular sample are described in any one of Liston/Driscoll, Horne '299, Easy Diagnostic, Parallel, and

Tilzer. Each of these references, published in the mid 1980's, describe an instrument that used bar codes to drive an automated process.

16. As explained in my Original Report, all the elements of the disputed claims are disclosed in the combination of Liston/Driscoll and JP '957. It is also clear from my discussion of Horne '299 and Sugaya '762 above that all the elements of the disputed claims are disclosed in Liston/Driscoll combined with Horne '299 or Sugaya '762. Liston/Driscoll, Horne '299, Easy Diagnostic, Parallel, and Tilzer all demonstrate that it was known prior to the '861 filing date that bar codes could be used to drive an automated biological processing apparatus.

17. As stated in the Background section of the '861 patent (and further discussed during prosecution of the '861 patent) the problems addressed by the method of the disputed claims include: (a) increasing throughput of the process, (b) permitting random placement of samples, (c) permitting different procedures to be performed on individual slides, and (d) improving accuracy and repeatability by minimizing the potential influence of human error. Each of these problems had already been addressed and overcome in the clinical chemistry labs years earlier. They were overcome (and the solution commercialized) prior to the '861 filing date by using bar codes to identify samples and reagents and to instruct the computer-controlled instrument what test procedure to apply to each sample. This is demonstrated in the numerous prior art references discussed in my reports. A person of ordinary skill would have been aware of the technology embodied in these earlier clinical chemistry analyzers and would have implemented this technology in the development of a process for dispensing reagents onto slides in a manner that overcomes these same problems. Indeed, from my own experience at the time, and as confirmed by the documents that I have reviewed, it is apparent to me that there was a trend throughout the 1980's toward the use of bar codes in biological processing apparatuses.

18. The documents that I reviewed in preparing this supplemental report and my Original Report discuss the advantages that can be realized by using bar codes in a computer controlled instrument. As further discussed below, these advantages addressed the same problems the inventors of the '861 patent stated were overcome by the method

recited in the disputed claims.

19. Liston '159 explains: "[a]nother significant advantage of the automated analysis system of the present invention is that it permits the effective use of a microprocessor-controlled loading and transfer assembly for presenting to the analyzer containers having the samples to be tested." Liston '159, col. 4, lns. 49-53. Driscoll et al explains that "[s]ample entry is totally random" and that bar codes provide "positive sample identification." Driscoll et al. at 1609.

20. JP '957 explains that the invention facilitates automation of the slide preparation process, that the glass slides can be arranged randomly, and that bar code identification makes it possible to dye many samples in a group. [VEN 015306]

21. The advantages described by Tilzer include reduced workload and reduced errors. Tilzer's system provides "[a] random-access chemistry analyzer for 'stat' as well as routine testing." Tilzer at p. 1200. In particular, Tilzer states that "[s]ervice has improved dramatically by not batching routine specimens but running all tests as they arrive in the laboratory." Id. Tilzer further explains that "[t]he benefits of integrating LIS-generated bar code-labeled specimens with new chemistry analyzers are reduction of workload, improved service, [and] decreased specimen labeling errors ...." Tilzer at 1201. Tilzer also states that the "bar-coded collection tube . . . allows for the continuous processing of samples." Id.

22. JP '165 (discussed in my Original Report) explains that bar-coded reagent containers "[eliminate] information entry mistakes and reagent placement mistakes." [VEN 015317]. JP '165 further states:

> [A]ccording to the present invention, entry mistakes would not occur which could occur in prior art when information regarding where reagents are placed is entered using a keyboard, or placing mistakes would not occur which could occur in prior art when reagents are placed on [a] reagent cassette. . . . [I]n the case of the present invention, a reagent bottle can be placed at any position on a reagent cassette, thereby simplifying reagent bottle placement operations.

[VEN 015318].

23. Horne '299 explains that "[a]ny cartridge may be inserted or removed at

will without disturbing any of the other cartridges and without stopping rotation of the rotor." Horne '299, col. 4, lines 11-13. As I explained above, this random access ability was due to the use of bar codes on the reaction slides and eliminated the wasted time of prior art apparatuses. Horne '299 also explains that another disadvantage obviated by the invention related to "the throughput of samples." Horne '299, col. 3, lines 23-29 and 47-48. Reducing wasted time would increase throughput.

24. Easy Diagnostic is a "random access system" in which bar codes on the reaction cuvettes "automatically program all instrument parameters including test selection, sample/diluent selection and addition . . . ." The advertisement describes a number of advantages of the system:

- The EASY™ Analyzer and bar-coded cuvettes allow walk-away operation resulting in significant time savings and increased productivity.
- Reagent preparation, system startup protocols, and reagent waste are virtually eliminated.
- The EASY™ Analyzer gives immediate results 24 hours a day to provide fast, accurate results . . . ."

25. Parallel describes "Four Easy Steps to Rapid Reporting" where the first step is "attach [a] bar code label to [a] sample tube" and system includes "the schedule of tests and the patient identification number encoded into the bar code label."

26. The numerous advantages of using bar codes described in the prior art would have motivated a person of ordinary skill in the art to incorporate bar codes into a computer-controlled process for dispensing reagents onto slides.

27. The fact that bar code technology had been successfully implemented in clinical chemistry analyzers (with much higher throughput volumes than histology instruments) to identify samples and cause the instrument to perform the correct procedure on each sample would indicate to me as one of skill in the art that bar code technology could also be successfully implemented in histology instruments.

Dated: 2/17/2005

Doug Koebler

Exhibit A to Supplemental Expert Report Regarding 6,352,861

Document	Bates Number
Horne, U.S. Patent Number 4,430,299.	VBS 14345-61
Rappoport, Arthur, E., "If Bar Codes Work in Supermarkets, It Should Be Great for Medicine," Pathologist, February 1985.	VEN 15346-47
Advertisement: "The Age Of Easy Diagnostic Testing," EM Diagnostic Systems, Inc., as published in Clinical Chemistry, Vol. 31, No. 6, 1985.	VBS 14390-91, 14397
Advertisement: Abbott Spectrum, as published in Clinical Chemistry, Vol. 3, No. 31, 1985.	VBS 14387, 14393, 14400
Advertisement: "Parallel Analytical System," American Monitoring Corporation, as published in Clinical Chemistry, Vol. 31, No. 1, 1985, p. 20A.	VBS 14388, 14399
Sugaya, U.S. Patent No. 4,800,762.	VBS 14411-16

Certificate of Service

I hereby certify that the foregoing **SUPPLEMENTAL EXPERT REPORT OF DOUG KOEBLER REGARDING U.S. PATENT NO. 6352861** was served via facsimile and Federal Express, on February 18, 2005, on the following individual:

Roger Chin
Wilson Sonsini Goodrich & Rosati
650 Page Mill Raod
Palo Alto, CA 94304-1050

DATED: February 18, 2005

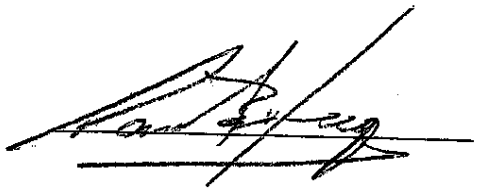

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EXHIBIT G

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

VISION BIOSYSTEMS (USA) TRADING, INC., Plaintiff, v. VENTANA MEDICAL SYSTEMS, INC., Defendant.	CIVIL ACTION NO. 03-CV-10391-GAO

SECOND EXPERT REPORT OF DAVID G. HICKS, M.D.

1. I am the Section Head of Surgical Pathology, and Co-Section Head of the Morphologic Molecular Pathology Laboratory, at the Cleveland Clinic Foundation. Previously, I was an Associate Professor in the Department of Pathology and Laboratory Medicine, with a joint appointment at the Cancer Center, at the University of Rochester School of Medicine, and an Attending Physician at the University of Rochester Medical Center.

2. I serve on the editorial board of the Journal of Bone and Joint Surgery, and previously served on the editorial board of the International Journal of Surgical Pathology. I also serve as an ad hoc reviewer for the Journal of Cancer, the American Journal of Pathology, Breast Cancer, and Clinical Cancer Research. I am a member of the United States and Canadian Academy of Pathology, and the College of American Pathology, and a former member of the Eastern Cooperative Oncology Group. I am a Diplomat of the American Board of Pathology, and am licensed to practice medicine in Pennsylvania, New York, and Ohio.

3. Further details about my qualifications are set forth in my prior report submitted in this case. If called as an expert witness in this matter, I anticipate that my testimony may concern the matters addressed below. My anticipated testimony may be affected by the production of additional information and/or positions plaintiff takes on the topics set forth in this report. I have been informed that plaintiff may communicate at least some of those positions to defendant some time after this report is prepared, such as in the form of deposition testimony to be given by its experts. After I have an opportunity to review those materials, I may amend or supplement this report.

4. In connection with formulating the opinions set forth in this report, I have reviewed the Supplemental Expert Report of Doug Koebler Regarding U.S. Patent No. 6,352,861 ("Supplemental Koebler Report"), materials identified in that report, the Court's Memorandum and Order dated September 30, 2004, and materials identified in my prior report.

5. I have been informed that claims 1, 2, 3, 5, 6 and 8 (the "asserted claims") of the '861 patent are at issue in this case. These claims all concern dispensing reagents onto a slide. These slides are used to support thin tissue sections for microscopic examination and interpretation. The end product of the slide staining is directed to the anatomic pathologist, who is responsible for examining stained tissue samples and rendering a diagnostic interpretation based on the morphologic features and pattern of staining in the tissue.

6. The Supplemental Koebler Report, in paragraph 4(b), cites an article from "a journal directed to pathologists" by A.E. Rappoport that deals with bar codes ("Rappoport article"). This generalized reference to "pathologists" fails to take into account the very different disciplines that fall under the umbrella of pathology. The Rappoport article, as Mr. Koebler acknowledges, concerns "laboratory and blood bank patient specimens" and "laboratory

management." This is clearly directed to a *clinical* pathologist who is responsible for running a clinical laboratory or a blood bank. Likewise, the other references Mr. Koebler identifies in his report on pages 2-3 also describe instruments that are designed for use in clinical laboratories. These references are is not directed to and do not make reference to the particular needs and requirements of an *anatomic* pathologist, who is the target audience for the methods of the asserted claims.

7. The clinical chemistry laboratories largely focused on obtaining quantitative measurements, such as the presence and amount of particular analytes in fluid samples. The automation in the clinical laboratory was driven in large part by the quantitative nature of measurements that were susceptible to high volume, high throughput, automated measurement. For example, U.S. Patent No. 4,430,299 ("Horne patent") provides a detailed calculation of the large number of quantitative readings that the device can obtain (col. 9, lines 21-38). While this may be important to needs and requirements of the clinical chemistry laboratory, such automated data acquisition is irrelevant to the evaluation of stained slides performed by an anatomic pathologist. The end result of tissue sample slide staining is not a quantitative measurement, but rather, it is an anatomic pathologist's assessment and interpretation of the presence of disease based on specific cell types present, staining reactions, and the complex morphological features of the tissue. In light of these marked differences, I disagree with the assertion in paragraph 27 of the Supplemental Koebler Report that the use of bar code technology in "clinical chemistry analyzers" would have made the asserted claims of the '861 patent obvious. To the contrary, a person with ordinary skill in the art (as described in paragraph 7 of my prior report) would recognize that the needs and requirements of the clinical chemistry laboratory (including the

focus on "higher throughput volumes" and quantitative measurements) was not pertinent to the end user of the asserted claims.

8. A further difference between the prior art in the Supplemental Koebler Report and the '861 patent is illustrated by the Horne patent and U.S. Patent No. 4,800,762 ("Sugaya patent"). The "cartridge 22" in the Horne patent and the chemical assay "slide 5" in the Sugaya patent have a very different function than the microscope slide called for by the asserted claims of the '861 patent. The cartridge/slide of Horne and Sugaya would be read by a photoanalyzer, which would obtain quantitative measurements of color change. (Horne patent, col. 3, lines 51-58; Sugaya patent, col. 1, lines 31-39.) They were designed to hold the detection chemistry onto which the patient's sample was dispensed. No reagents are dispensed onto the cartridge/slide. That is the opposite of the function of the microscope slide in the '861 patent, which supports a tissue sample onto which reagents are dispensed. A microscope slide allows for the placement of a very thin and delicate cross-section of a tissue specimen under a microscope for morphological evaluation. Unlike the sample that must be dispensed onto the cartridge/slide, the sample on a microscope slide is fixed to the slide, cannot be readily transferred, and is preserved as part of the permanent patient record. In fact, Mr. Koebler's observation (paragraph 4(a)) that the cartridge/slide "serves the same purpose as a cuvette" underscores the differences in intended use between the cartridge/slide and the microscope slides used in the asserted claims of the '861 patent. Like other clinical laboratory specimens, the cartridge/slide is disposed of after analysis, unlike microscope slides which are preserved as part of the patient record after interpretation.

9. Paragraph 17 of the Supplemental Koebler Report asserts that a person of ordinary skill in the art "would have implemented this technology" from the clinical chemistry

analyzers "in the development of a process for dispensing reagents onto slides." This speculation fails to account for the differences between the clinical chemistry instruments and the needs and requirements of the anatomic pathologist. In fact, the variety of automation available in the clinical laboratories, as described in Mr. Koebler's reports, underscores the skepticism and lack of obviousness to apply Ventana's automated approach to anatomic pathology. Furthermore, Mr. Koebler's contention is at odds with the historical development in this field. The utility of IHC staining was recognized by the late 1960's to early 1970's, and had been recognized by the beginning of the 1980's as one of the most powerful tools complementing and extending morphologic tissue analysis. (Brooks, Immunohistochemistry of Soft Tissue Tumors: Progress and Prospects, *Human Pathol.*, 13:969-974, 1982.) There were laboratories in large university-based hospitals that devoted considerable time, effort, and other resources to developing and implementing IHC capabilities. There also were substantial financial and technical resources available to industry, including some companies who manufactured the clinical analyzers like the ones described in Mr. Koebler's reports. Even though a great need for improvements to and wider availability of IHC slide staining existed for years before the '861 patent, and resources were available, there was no successful automated slide staining instrument of the type described in the '861 patent prior to 1990. Had Ventana's approach been obvious, as asserted in paragraph 17 of the Supplemental Koebler Report, automated slide staining techniques described in the '861 patent would have been available at least a decade earlier.

10. I disagree with the contention made in paragraph 17 of the Supplemental Koebler Report that "problems addressed by the method of the disputed claims ... had already been addressed and overcome in the clinical chemistry labs years earlier." Once again, the

development history of automated slide stainers argues against this contention. Since the 1990's, Ventana's automated slide staining systems have met with great success and popularity among anatomic pathologists, and resulted in the expansion of the base of immunohistochemistry laboratories to community-based hospitals. These successful instruments included the ES, NexES, BenchMark, and Discovery. I have had first-hand experience with each of these instruments, and I know that they are used to perform methods that include each of the steps set forth in claims 1 and 5 of the '861 patent. By automating steps previously performed manually by technical staff and providing the advantages described in my prior report, the functionality as described in those claims contributed to the success of the Ventana instruments among the diagnostic anatomic pathology community.

David G. Hicks, M.D.

I hereby certify that a true copy of the Second Expert Report of David G. Hicks, M.D. was served upon the attorneys of record for plaintiff Vision BioSystems (USA) Trading, Inc. by facsimile and U.S. mail on March 11, 2005:

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September 12, 2005

Via Facsimile

Nicole Stafford, Esq.
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8911 Capital of Texas Highway North
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Austin, Texas 78759-8497

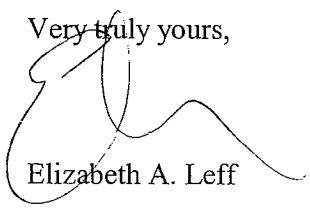
Re: Ventana Medical Systems, Inc. v. Vision BioSystems Inc.
District of Mass. 05-CV-10614-GAO
Our Ref.: 2961-102

Dear Nicole:

To avoid any dispute regarding our agreement concerning validity discovery, I set out below the bates ranges of documents which Ventana produced in Vision II and which Vision believes go to validity. Please confirm that Ventana will not rely on any of these documents at trial in exchange for Vision's agreement not to call Dr. Horne or anyone not disclosed in Vision I as a witness to testify on matters of patent validity.

VEN 1026514 – VEN 1029158
VEN 1029159 – VEN 1029230
VEN 1029238 – VEN 1029239
VEN 1029937 – VEN 1030917

Very truly yours,



Elizabeth A. Leff

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EXHIBIT

I

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April 12, 2007

VIA E-MAIL

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Westech 360, Suite 3210
Austin, Texas 78759-7247

Re: Vision BioSystems (USA) Trading, Inc. v. Ventana Medical Systems, Inc., 03-CV- 10391 GAO (D. Mass.); Ventana Medical Systems, Inc. v. Vision BioSystems, Inc., 05-CV-10614 GAO (D. Mass.) Our Ref.: 13497/1

Dear Nicole:

Thank you for your letter of April 10, 2007, to which I respond as follows.

As to code inspection, in our conversation on April 10, 2007, I said that I did not believe that Vision would have any objection to permitting a code inspection as was conducted previously. The draft stipulation that you had sent me earlier, on April 5, 2007, included a provision that Vision would make code available for inspection "promptly." Given the logistics, I stated that I was not sure how "prompt" that could be, and I questioned whether it was necessary to include specific reference to a code inspection in our scheduling stipulation. I stated that I would need to coordinate with the client regarding such an inspection, and it did not seem to make sense to hold up the agreement on scheduling deadlines while we tried to coordinate matters regarding a code inspection.

In any event, we have now consulted with Vision on the matter. As I suspected, Vision has no objection to permitting a code inspection as was conducted previously. It is just a matter of making the necessary arrangements for it to happen, which, as I suspected, will take some time.

Further, with respect to the code inspection as well as to supplementation of document productions, as I mentioned to Roger Chin in February, there have been some changes to the Bond – OCR since the last discovery materials were provided. Accordingly, we will be providing documentation relating to the changes and the current version of the Bond – OCR shortly. Vision will make the code from the current Bond – OCR available under similar arrangements as the prior code inspection.

In our conversation on April 10, 2007, I informed you that we were considering the proper subject matter scope of the upcoming discovery period. Specifically, the draft stipulation you sent me stated that the upcoming discovery would be limited to the issue of infringement only. In our conversation, I stated that we are considering that some additional discovery would be appropriate. I agree that we should try to come to some agreement as to the scope of discovery and, to the extent that we cannot, the issue should be brought to the Court's attention as soon as possible.

In this regard, please let me know Ventana's responses regarding the following issues:

(1) Injunctive Relief – As you are no doubt aware, in ebay v. Merc Exchange, 547 U.S. 206 (2006), the Supreme Court held that the Federal Circuit erred in applying a "general rule" that a permanent injunction should issue when infringement and validity are found. In ebay, the Supreme Court held that the determination of whether to issue a permanent injunction should be made according to traditional principles of equity requiring a party seeking an injunction to demonstrate: (1) that it has suffered an irreparable injury, (2) that remedies available at law are inadequate to compensate for that injury, (3) that considering the balance of hardships between the plaintiff and defendant, a remedy in equity is warranted, and (4) that the public interest would not be disserved by a permanent injunction.

Accordingly, assuming Ventana still intends to seek an injunction, under the ebay case, discovery relating to the factors underlying an injunction is appropriate. In this case, because the remedies phase of trial (damages and willfulness) is bifurcated from the liability phase of trial, Vision's view is that discovery relating to injunctive relief should be deferred to occur with other discovery relating to remedies, i.e., damages and willfulness, and that, in the event liability is found, the determination of whether or not to grant injunctive relief should take place on the same schedule as the determination of damages.

Please let us know whether Ventana agrees that the issue of the availability of injunctive relief is one that is not part of the liability phase of the case but is instead part of the remedies part of the case, along with the issues of damages and willfulness. That is, will Ventana agree that, should Ventana prevail at the liability trial, Ventana will not request injunctive relief until the time of the remedies (damages/willfulness) trial?

(2) Objective Indicia Relating to Obviousness/Nonobviousness

(a) Commercial Success – Ventana's experts have relied on "commercial success" as allegedly evidencing nonobviousness of the claimed invention. In this regard, Ventana has relied on the alleged success of machines first marketed many years after the

application for the patent in suit was filed (e.g., Discovery, BenchMark, BenchMark XT). Please let us know whether Ventana will agree to provide a supplementation of discovery relating to the issue of commercial success. In this regard, we will agree to provide a supplementation of Vision's document production and discovery responses to provide updated information from Vision relating to this issue.

(b) Licensing – To the extent there have been any licenses of the '861 patent or any offers to license the '861 since discovery last took place on the issue, please let us know whether Ventana will agree to provide a supplementation of discovery to provide this information.

The above issues relate to the scope of fact discovery. With respect to expert discovery, we will get back to you with our position shortly. In the meantime, please let me have your responses to the above questions.

Sincerely,

Douglas E. Ringel

656095

EXHIBIT

J

KENYON & KENYON LLP
Intellectual Property Law

Douglas E. Ringel
Direct 202.220.4225
dringel@kenyon.com

1500 K Street, N.W.
Washington, D.C. 20005-1257
202.220.4200
Fax 202.220.4201

April 16, 2007

VIA E-MAIL

Nicole W. Stafford, Esq.
Wilson Sonsini Goodrich & Rosati
8911 Capital of Texas Hwy. North
Westech 360, Suite 3210
Austin, Texas 78759-7247

Re: Vision BioSystems (USA) Trading, Inc. v. Ventana Medical Systems, Inc., 03-CV- 10391 GAO (D. Mass.); Ventana Medical Systems, Inc. v. Vision BioSystems, Inc., 05-CV-10614 GAO (D. Mass.) Our Ref.: 13497/1

Dear Nicole:

This is in response to your letter of Friday, April 13, 2007, and addresses the issues of (1) injunctive relief, and (2) expert discovery relating to obviousness.

(1) Injunctive Relief

As you pointed out to me in your letter of April 10, 2007, the parties previously agreed that the only discovery to be taken in the *Vision II* case prior to the liability trial was on the issue of infringement. Other discovery was deferred until after the liability trial. Indeed, in your letter of July 26, 2005, addressed to Elizabeth Leff, you stated, "We also agree that bifurcation of damages is appropriate and discovery related to damages, irreparable harm, and balancing of the harms is not necessary or appropriate at this time." The stipulation signed by the parties and filed with the Court on August 9, 2005, reflects this agreement, stating "1. The parties may seek discovery relevant to Ventana's claim that the Bond OCR infringes the '861 patent and such other topics as permitted by Court Order … ."

The Supreme Court issued its ruling in the *ebay* case on May 15, 2006. If Ventana believed that the *ebay* case meant that discovery and trial relating to the injunction issue should

take place with the liability phase rather than the remedies phase, Ventana could have and should have raised the issue at that time.

Indeed, after the Federal Circuit ruled in the *Biogenex* case on December 29, 2006, Roger Chin and I exchanged several e-mails and had several discussions leading up to the February 21, 2007, hearing before Judge O'Toole. At no point did Roger indicate that Ventana wanted to include the issue of injunctive relief as part of the liability phase. If he had done so, we could have raised the issue with the Court, and we would have sought to have it resolved in the context of setting the trial date. Instead, Roger represented to the Court of February 21, 2007, that Ventana's position was that discovery leading up to the liability trial should start "where we left off," with the only remaining liability discovery being on the issue of infringement of "the second accused device, the Bond OCR, [which] was the subject of fact discovery that the parties were wrapping up at the time."

Your follow-up communications were consistent with Roger's representation that the upcoming trial is on liability only. Your e-mails of April 3 and 5 both included stipulations expressing Ventana's position that "fact and expert discovery is limited to the issue of infringement." Your letter of April 10 emphasized this position. You confirmed that "Ventana's agreement to the dates included in the attached stipulation was based on the scope of discovery in *Vision II* being limited to infringement by Bond – OCR."

Indeed, the injunction issue logically belongs with the damages issue. Much of the discovery relating to the propriety of an injunction, such as that relating to the irreparability of any alleged injury, the adequacy of other remedies, and the balance of hardships, overlaps significantly with the discovery that relates to damages. Both issues involve significant discovery relating to the market, sales, financials, etc. They involve overlapping witnesses not needed for liability discovery or trial. And, as with damages and the issue of willfulness, discovery and trial relating to the injunction issue is rendered completely unnecessary in the event of a finding of no liability.

Most importantly, though, is the issue of prejudice. Discovery relating to the *ebay* factors is significant and has not yet even begun. To ask Vision to start now and complete all necessary fact discovery relating to the injunction issue on the expedited schedule we have for the liability discovery is unreasonable and extremely prejudicial. The issue is simply too important and requires far too much discovery for Ventana to attempt now to belatedly inject it into the liability phase of the case.

(2) Expert Discovery Relating to Obviousness

In my letter of April 12, 2007, I indicated that I would get back to you with Vision's position regarding the proper scope of expert discovery for the liability phase of trial.

In our view, some limited additional supplemental expert discovery on the issue of obviousness is warranted, as described below. This supplemental expert discovery is warranted because, *inter alia*, (i) Ventana produced certain materials pertinent to obviousness subsequent to the prior discovery period on obviousness, (ii) some relevant fact discovery remains that bears on

the issue of obviousness, particularly relating to the issue of objective indicia of obviousness/nonobviousness (secondary considerations), as reflected in my letter of April 12 and your agreement of April 13, (iii) the current law of obviousness is being considered by the Supreme Court in the *KSR* case, and the Federal Circuit has had further significant statements relating to the obviousness inquiry in the *Alza*, *Dystar* and *Kahn* cases, (iv) the Court would benefit from having a complete record on the issue of obviousness, including all pertinent references and balanced testimony wherein both sides present testimony from pathologists, (v) there is a strong public interest in having validity of patents correctly adjudicated, and (vi) there is no prejudice to Ventana from the limited discovery we propose.

Specifically, we propose that Vision would serve supplement expert reports on the obviousness issue, as follows:

(i) from Dr. Ulysses Balis (c.v. attached), addressing the reports of Dr. Hicks, objective indicia of obviousness/nonobviousness (secondary considerations), and giving the perspective of a pathologist relative to the issue of obviousness as presented in the reports of Mr. Koebler; and

(ii) from Mr. Koebler, addressing the issue of objective indicia of obviousness/nonobviousness (secondary considerations), as well as U.S. Patent No. 5,122,342 to McCulloch, as they relate to the issue of obviousness (in connection with other evidence previously addressed by Mr. Koebler).

Our proposal would be to set a time for this supplementation to occur. If the Supreme Court has ruled in the *KSR* case by that time, the experts would include the appropriate analysis within the analytical framework set by the Supreme Court. If the Supreme Court has not ruled in the *KSR* case by that time, the experts would include the appropriate analysis under the *Alza*, *Dystar* and *Kahn* cases, with possible supplementation necessary depending on how the Supreme Court rules in *KSR*.

With respect to the issue of objective indicia of obviousness/nonobviousness (secondary considerations), both sides agree that additional fact discovery is yet to take place. Obviously if the parties are to present expert testimony at trial relating to obviousness, it needs to take into account all relevant evidence on the issue, including the new evidence.

With respect to Dr. Balis's report and the rebuttal of the reports of Dr. Hicks, Dr. Balis will simply be responding to evidence and arguments introduced by Ventana. We believe that having both sides present testimony from pathologists is in the interest of fairness and presents the Court with a more complete and balanced record. There is no prejudice to Ventana, as it was Ventana that introduced the pathologist perspective through the reports of Dr. Hicks. Moreover, we anticipate that Dr. Balis will be submitting an expert report relating to the issue of noninfringement, and he can be deposed once with respect to the entirety of his expected testimony. Thus, his obviousness report will not require an additional deposition.

With respect to the McCulloch '342 patent, as I am sure you are aware, the McCulloch '342 patent was the subject of a number of documents that were produced by Ventana after obviousness discovery took place in our case. *See*, *e.g.*, documents produced September 21,

2005. While there was mention of the reference in earlier documents, the documents produced on September 21, 2005, contain detailed information relevant to the pertinence of the McCulloch '342 patent to the '861 patent at issue in this case. Moreover, there is no prejudice to Ventana in the addition of this reference as Ventana has been fully aware of it through the *Biogenex* case, has already had full discovery with respect to it, and has already addressed it with its own expert analysis in the *Biogenex* case.

As can be appreciated, Vision's proposal is very narrow, requires no additional fact discovery beyond that already agreed by the parties, presents no issue that is new to Ventana, and requires very limited actual expert discovery beyond that which is otherwise needed for the upcoming liability trial. The limited additional expert discovery proposed can easily be completed within the schedule to which the parties have agreed. Accordingly, please let me know whether Ventana agrees to this supplementation as we propose.

Finally, with respect to Dr. Balis, in accordance with paragraph 4(d) of the Stipulation and Protective Order, please find enclosed Dr. Balis's signed agreement to be bound by the Protective Order. Dr. Balis has not had any past employment or consulting relationship with any party or related company that has conducted research or development or produces or sells products in the field of instruments for immunohistochemistry or in situ hybridization. Please let me know whether Ventana has any objection.

Sincerely,

Douglas E. Ringel

656438

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

VISION BIOSYSTEMS (USA) TRADING INC., Plaintiff, v. VENTANA MEDICAL SYSTEMS, INC., Defendants.	Civil Action No. 03-CV-10391-GAO

AGREEMENT TO BE BOUND BY PROTECTIVE ORDER

I, Ulysses J Balis being duly sworn, state that:

1. My residence address is 3503 Blue Heron Ct. Ypsilanti, MI 48198
2. My present employer is U. of Michigan and the address of my present employment is 1300 Catherine St., Ann Arbor, MI 48109
3. My present occupation or job description is Pathologist / Informaticist
4. A copy of my *curriculum vitae* is attached hereto.
5. I have carefully read, and I understand, the provisions of the Protective Order entered in this case, and I will comply with all provisions of the Protective Order.
6. I will hold in confidence and not disclose to anyone not qualified under the Protective Order any CONFIDENTIAL INFORMATION or any words, summaries, abstracts, or indices of CONFIDENTIAL INFORMATION disclosed to me.
7. I will return all CONFIDENTIAL INFORMATION and summaries, abstracts, and indices thereof that come into my possession, and documents or things that I have prepared relating thereto, to counsel for the party for whom I was employed or retained.

I declare under penalty of perjury that the foregoing is true and correct.

Date: 4.13.2007

1592-364\...\protective order.wpd

CURRICULUM VITAE

Name: Ulysses Gregory John Balis

Email: ul@balis.com

Education:

9/1984 - 5/1987	Duke University, Durham, NC. B.S., (Computer Engineering – dual-major program)
9/1984 - 5/1987	Duke University, Durham, NC, B.S., (Biology – dual-major program)
8/1987 - 5/1991	University of South Florida, Tampa, FL, M.D.

Postdoctoral Training:

7/1991 - 6/1996	Residency in Combined Anatomic / Clinical Pathology University of Utah, Salt Lake City, UT
7/1996 - 6/1998	Postdoctoral Research Fellow Whitaker Foundation B.E.R.E. Program The Center for Engineering in Medicine, Massachusetts General Hospital and Harvard University Health Sciences and Technology Program
7/1998 - 6/2000	Research Associate Shriners Burns Hospital, Boston Unit and The Center for Engineering in Medicine, Massachusetts General Hospital
7/1996 - 6/2000	Research Fellow in Surgery (Bioengineering), Harvard University
7/1996 – 6/2000	Research Fellow in Surgery (Bioengineering), Massachusetts General Hospital

Licensure and Certification:

1991	National Board of Medical Examiners
1991- 1996	Physician, State of Utah
2000	Physician, Commonwealth of Massachusetts

Academic Appointments:

7/2000 – 8/2002	Instructor in Pathology, Harvard University
9/2002 - present	Assistant Professor of Pathology and Computer Engineering; Harvard Medical School

Academic Administrative Appointments

7/2000 -	Chief of Pathology and Laboratory Services, Shriners Hospital for Children, Boston Burns Unit
1/2002-	Director of Pathology Informatics, Massachusetts General Hospital
1/2004 – 4/2005	Acting Chief Information Officer, Shiners Hospital for Children, Boston Burns Unit
7/2000-	Directory of Laboratory Services, Shriners Hospitals for Children - Boston Burns Unit.

Hospital and Affiliated Institution Appointments

8/1992 - 6/1996	Founding Medical Director Core Instrumentation and Image Processing Laboratory Associated Regional and University Pathologists, Inc., Salt Lake City, Utah
7/1993 - 6/1996	Assistant Medical Director Flow Cytometry Clinical Laboratory. Associated Regional and University Pathologists, Inc., Salt Lake City, Utah
7/2000 -	Assistant in Pathology and Computer Science, Massachusetts General Hospital

Scientific Activities

1998 - 2000	Voting Member, Synoptic Nomenclature of Medicine (SNOMED) Editorial Board, College of American Pathologists
1999 -	Ad hoc reviewer; topics in telemedicine, tissue engineering, Journal of the American Medical Association
2000 -	Ad hoc reviewer; topics in quantitative PCR, Journal of Clinical Chemistry

2000 - 2003	Committee Advisor, Synoptic Nomenclature of Medicine (SNOMED) Editorial Board, College of American Pathologist
2003 -	Reviewer, Bioinformatics section, BioMed Central online publications

Grant Support

1990-1991	Intramural Departmental Grant, University of South Florida Department of Pathology. PI, *Wide Area Network (WAN) Telepathology Linkage of the James A. Haley Veterans Hospital and the Bay Pines Veterans Hospital*. $16,000.
1992-1996	Intramural Departmental Grant, University of Utah Department of Pathology / Associated Regional and University Pathologists, Inc. Founding Clinical Medical Director, *Core Instrumentation and Image Processing Laboratory*, $348,000.
2001-2006	Investigator, Shared Pathology Information Network (SPIN), National Cancer Institute (1U01CA091429-01); 20% Effort. P.I.: Zak Keohane, MD, PhD. $6,140,210 (5 years).
2000-	Principle Investigator, Danafarber Harvard Cancer Center (DFHCC) Virtual Specimen Locator Initiative (Intramural). 15% effort (5 years).
2005-	Investigator, A Novel Breast Cancer Biomarker. National Cancer Institute (1R01CA112021-01); 5 % effort. P.I.: Dennis Sgroi, M.D.
2005-	Investigator, Living Cell Arrays for Real Time Functional Genomics , National Institute Of Allergy And Infectious Diseases (1R01AI063795-01) 10 % effort. P.I.: Martin L. Yarmush, M.D., Ph.D.
2006-	Consultant: Inflammation and the Host Response to Injury (5U54GM062119-05) 10% effort. P.I. Ronald Tompkins, M.D., Sc.D.

Military Service

None

Honors and Awards

1982	Early Acceptance Honors Program Recipient, University of South Florida
1982	State of Florida Governor's Award of Distinction for Outstanding Academic Achievement
1984	Deans List, Duke University
1991	Annual Award for Excellence in Pathology and Laboratory Medicine, University of South Florida College of Medicine
1995	Presidential Service Award, College of American Pathologists

1996	Whitaker Foundation Bioengineering Fellowship Recipient Massachusetts General Hospital and Harvard Medical School
2000	Lansky Award, College of American Pathologists
2003	Society for Ultrastructural Pathology, Award for best ultrastructural abstract, United States and Canadian Academy of Pathology Annual Meeting.
2003	Best Scientific Session: for *Controlled Vocabularies, Decision Support and Outcome Research*, APIII Annual Meeting (Advancing Practice, Instruction and Innovation Through Informatics (Pittsburgh, October 6-8)
2003	Invited Keynote Speaker, Healthcare Informatics Society of Australia, Pathology Information Technology World Symposium. Gold Coast, Australia, September.
2005	Invited Visiting Fellow and Keynote Speaker, Australian Royal College of Pathologists; Pathology Update Meeting.
2005	Invited Visiting Fellow and Keynote Speaker Current Update in Telepthology, Provincial Laboratory Coordinating Office (PLCO); British Colombia, Canada.

Memberships in Professional Societies

1991-	College of American Pathologists, Committee Chair and Council Member
1992	World Congress of Non-linear Analysts, Member
1994-	Institute of Electrical and Electronic Engineers (IEEE), Member
1998-	IEEE Computer Society, Member
1998-	American Foundation for Greek Language and Culture (www.afglc.org)
2000-	Association of Pathology Informatics, Founding Member
2000-	American Medical Association, Member
2000 - 2006	Massachusetts Medical Society, Member

Teaching Activities

2000-	Massachusetts General Hospital Department of Pathology: Ongoing development and Extension of a Pathology Informatics Curriculum for the Residency Program
2000-	Massachusetts General Hospital Department of Pathology: Resident teaching of gastrointestinal surgical pathology.
2001-2006	Core Faculty: Massachusetts Institute of Technology - Harvard HST Program: *HST505: Laboratory in Molecular and Cellular Sciences* – Advanced tutorials in scientific image acquisition and analysis; annual workshop/symposium.

Extramural Invited Presentations

Invited Lecture. Distributed Imaging with a Digitizing Videodisk Fileserver. Slice of Life V Workshops, Salt Lake City, Utah, 1992

Invited Lecture. Identification and Quantification of Attractor Metamorphosis in Digitized Histopathologic Images. Plenary Section: "Asymptotic Behavior of Nonlinear Systems: Attractors and Confinors: Application to Biology." First World Congress of Nonlinear Analysts, Tampa, Florida, 1992

Invited Lecture. Digital Image Resolution and Diagnostic Accuracy in Hematopathology. Spring ASCP/CAP National Meeting, 1993

Roundtable Seminar. The Digital Pathology Workstation, Spring ASCP/CAP National Meeting, 1993

Invited Lecture. Telepathology and Image Transfer. Fall ASCP/CAP National Meeting, 1993

Roundtable Seminar . The Digital Pathology Workstation. Fall ASCP/CAP National Meeting, 1993

Seminar, twice presented. Image Processing and Analysis for the Surgical Pathologist. Moderator and Presenter. Spring and Fall ASCP/CAP National Meetings, 1994

Invited Workshop. The Pathologist's Workstation. Fall ASCP/CAP National Meeting, 1994

Seminar, twice presented: Image Processing for the Pathologist. Moderator and Presenter. Spring and Fall ASCP/CAP National Meetings, 1995

Invited Lecture. DICOM and Pathology. Fall ASCP/CAP National Meeting, 1995

Roundtable Seminar. The Digital Pathology Workstation. Fall ASCP/CAP National Meeting, 1995

Invited Demonstration. Pathologists in the Cockpit; Demonstration of Real-time robotics telepathology at the Department of Pathology, University of Utah. *Infofair '96 - Becoming Digital.* Spencer S. Eccles Health Sciences Library, Salt Lake City, 1996

Seminar. Advanced Tutorials in Image Processing and Analysis for Pathology. Spring ASCP/CAP National Meeting, 1996

Invited Lecture. Global World Wide Web for Pathologists. Fall ASCP/CAP National Meeting, 1996

Invited Lecture. Implementation Issues in Telepathology. University of South Florida Department of Pathology Grand Rounds, 1997

Workshop Seminar. Telepathology and Standards for Enhanced Productivity. Spring ASCP/CAP National Meeting, 1997

Seminar. Global World Wide Web. Spring ASCP/CAP National Meeting, 1997

Roundtable Seminar. Desktop Imaging for the Pathologist. Fall ASCP/CAP National Meeting, 1997

Invited Seminar. Digital Pathology. Fall ASCP/CAP National Meeting, 1997

Invited Roundtable Seminar. Desktop Imaging for the Pathologist. Spring ASCP/CAP National Meeting, 1998

Invited Lecture. The Internet Demystified: Technical Aspects of TCP/IP and HTML Interoperability. Spring ASCP/CAP National Meeting, 1998

Invited Seminar & Workshop. Telefest! State of the art issues in telepathology with demonstrations. Spring ASCP/CAP National Meeting, 1998

Invited Lecture. Informatics Weekend Resident Symposium. Fall ASCP/CAP National Meeting, 1998

Invited Lecture. Automated Synoptic Reporting. Fall ASCP/CAP National Meeting, 1998

Invited Lecture. Biotech and Infotech Opportunities for Pathologists. Fall ASCP/CAP National Meeting, 1998

Seminar. Laboratory Statistics You Will Actually Use. Fall ASCP/CAP National Meeting, 1998

Roundtable Seminar. Desktop Imaging for the Pathologist. Fall ASCP/CAP National Meeting, 1998

Invited Lecture. Telepathology Update. Pathology Grand Rounds. University of South Florida Health Sciences Center, Tampa, FL, 1998

Invited Lecture. Bioartificial Liver Technology in Review. Pathology Lecture Series. University of South Florida Health Sciences Center, Tampa, FL., 1999

Roundtable Seminar. Desktop Imaging for the Pathologist. Spring ASCP/CAP National Meeting, 1999

Invited Teleconference Seminar. A Primer on Digital Imaging. American Society of Cytopathology Teleconference, May 25, 1999

Roundtable Seminar. PERL programming for the Pathologist. Fall ASCP/CAP National Meeting, 1999

Roundtable Seminar. Desktop Imaging for the Pathologist. Spring ASCP/CAP National Meeting, 2000

Invited Lecture. State of the Art Digital Pathology, Southwest Florida Association of Pathology Grand Rounds Series, Sarasota, FL., June, 2000.

Roundtable Seminar: Desktop Imaging for the Pathologist. Fall ASCP/CAP National Meeting, 2000

Annual Course on Advanced Tutorials in Biological Image Analysis and Image Processing. HST505: *Laboratory in Molecular and Cellular Sciences.* Massachusetts Institute of Technology HST Seminar Graduate Program, Cambridge, MA., January, 2000 See: http://hst.mit.edu/servlet/ControllerServlet?handler=PublicHandler&action=viewCourse&courseID=HST+505&term=2003JA

Pathology Grand Rounds: Current A review of Clinical State of the Art in Bioartificial Liver Support Systems. Scripps Medical Center, April, La Jolla, CA, 2001

Annual Course on Advanced Tutorials in Biological Image Analysis and Image Processing. HST505: *Laboratory in Molecular and Cellular Sciences.* Massachusetts Institute of Technology HST Seminar Graduate Program, Cambridge, MA., January, 2001 See: http://hst.mit.edu/servlet/ControllerServlet?handler=PublicHandler&action=viewCourse&courseID=HST+505&term=2003JA

Invited Lecture, Images Are Not Enough: Integration of Data and Images In a Fully Integrated Electronic Medical Record System, University of Minnesota, Minneapolis, MN., June, 2001

Synthetic Microscopy for True Digital Signout: Roundtable Session. ASCP/CAP National Meeting, Philadelphia, PA, October, 2001

Web-Based Digital Microscopy. ASCP/CAP National Meeting, Philadelphia, PA, October, 2001.

Annual Course on Advanced Tutorials in Biological Image Analysis and Image Processing. HST505: *Laboratory in Molecular and Cellular Sciences.* Massachusetts Institute of Technology HST Seminar Graduate Program, Cambridge, MA., January, 2002 See: http://hst.mit.edu/servlet/ControllerServlet?handler=PublicHandler&action=viewCourse&courseID=HST+505&term=2003JA

Invited Lecture: Cognitive learning and educational digital imaging repositories. Group for Research in Pathology Education (GRIPE) Annual Meeting; University of South Florida, Tampa FL, January, 2002.

Invited Lecture, Standardization of Interoperable Pathology Reporting. APIII Annual Meeting. Pittsburgh, PA, October, 2002.

Invited Focus Group Participant: Tissue Microarray Application Data Exchange Standards. APIII Annual Meeting. Pittsburgh, PA, October, 2002.

Annual Course on Advanced Tutorials in Biological Image Analysis and Image Processing. HST505: *Laboratory in Molecular and Cellular Sciences.* Massachusetts Institute of Technology HST Seminar Graduate Program, Cambridge, MA., January, 2003 See: http://hst.mit.edu/servlet/ControllerServlet?handler=PublicHandler&action=viewCourse&courseID=HST+505&term=2003JA

Invited Keynote Speaker, Healthcare Informatics Society of Australia, Pathology Information Technology World Symposium. Gold Coast, Australia, September, 2003.

Invited Scientific Presentation: Automated Deidentification of Pathology Reports, Beckwith B, Kuo F, Balis UJ. APIII Annual Meeting. Pittsburgh, PA, October, 2003.

Annual Course on Advanced Tutorials in Biological Image Analysis and Image Processing. HST505: *Laboratory in Molecular and Cellular Sciences.* Massachusetts Institute of Technology HST Seminar Graduate Program, Cambridge, MA., January, 2004 See: http://hst.mit.edu/servlet/ControllerServlet?handler=PublicHandler&action=viewCourse&courseID=HST+505&term=2003JA

Invited Scientific Presentation: Implementation of a Region of Interest-Based Query Using Vector Quantization, Generalized Affine Class-based Vocabularies and Multimodal Chebyshev Polynomial Normalization to Retrieve Context-matched Imagery from Existing Digital Image Repositories, , Balis UJ. APIII Annual Meeting, Pittsburgh, PA, October, 2004.

Invited Presentation: Current Developments in Imaging and Informatics for the Practicing Surgical Pathologist. Harvard Medical School Current Concepts in Surgical Pathology. November 2004.

Annual Course on Advanced Tutorials in Biological Image Analysis and Image Processing. HST505: *Laboratory in Molecular and Cellular Sciences.* Massachusetts Institute of Technology HST Seminar Graduate Program, Cambridge, MA., January, 2005 See: http://hst.mit.edu/servlet/ControllerServlet?handler=PublicHandler&action=viewCourse&courseID=HST+505&term=2003JA

Invited Scientific Presentation: Region-of-Interest Based Differential Diagnosis Via the Use of Vector Quantization and N-Dimensional Bayesian Voronoi Mapping. Balis UJ. APIII Annual Meeting. Pittsburgh, PA. October. Lake Tahoe, NV, August 2005.

Invited Presentation: Current Developments in Imaging and Informatics for the Practicing Surgical Pathologist. Harvard Medical School Current Concepts in Surgical Pathology. November 2005.

Invited Keynote Speaker: Provincial Laboratory Coordinating Office of British Columbia Telepathology Symposium. "Telepathology: From Theory To Implementation." Vancouver, BC, December 7, 2005. http://www.plco.ca/news5.html

Annual Course on Advanced Tutorials in Biological Image Analysis and Image Processing. HST505: *Laboratory in Molecular and Cellular Sciences.* Massachusetts Institute of Technology HST Seminar Graduate Program, Cambridge, MA., January, 2006 See: http://hst.mit.edu/servlet/ControllerServlet?handler=PublicHandler&action=viewCourse&courseID=HST+505&term=2003JA

Invited Presentation: Lab Infotech Summit. "Searching Surgical Pathology Databases with Images Instead of Words." Las Vegas, NV, March 2, 2006. https://www.labinfotech.org/LIS2006/Conference_Agenda.php

Committee and Administrative Service

Institutional

2000 -	Co-director, MGH Division of Anatomic Pathology Website Development taskforce
2001-2002	Member, MGH Division of Anatomic Pathology AP Information System Search Committee.
2002-	Joint MGH/BWH Anatomic Pathology Implementation Task Force, Partners Healthcare Information Systems Division
2002-	Team Pathologist, MGH Division of Anatomic Pathology AP Information System Implementation Project (tandem project with Brigham and Woman's Hospital AP Information System Implementation)
2003-	Information System (SHCIS) Implementation; Acting CIO, Shriners Hospital for Children – Boston Burns Unit
2003-	Member, Standing Readiness Task force for Joint Commission Surveys, Shriners Hospital for Children, Boston Burns Unit

National and International

1992-1995	Member, Informatics Committee, College of American Pathologists
1993-1994	Liaison to ANSI/HISB (American National Standards Institute / Healthcare Information Standards Board),College of American Pathologists
1993-1994	Member, Cytology Proficiency Testing Advanced Technology Ad Hoc Search Committee,College of American Pathologists
1993-1996	Liaison to ACR/NEMA (American College of Radiology / National Electrical Manufacturers Association), College of American Pathologists
1994-1996	Member, University of Utah Health Sciences Center Telemedicine Outreach Committee
1994-1996	Founding Chair, Image Exchange Committee, College of American Pathologists
1994-1996	Adjunct Member, Council on Practice Management College of American Pathologists
1995-1996	Founding Member, World Wide Web Task Force, College of American Pathologists
1995	Member, Informatics Subcommittee for Revising the Information Systems Section of the Laboratory Inspection Checklist, College of American Pathologists
1996-1998	Liaison to ANSI/HISB (American National Standards Institute / Healthcare Information Standards Board), College of American Pathologists
1997-1998	Member, Informatics Committee,College of American Pathologists
1997-1998	Member, Informatics Subcommittee for Revising the Information Systems Section of the Laboratory Inspection Checklist, College of American Pathologists
1997-2004	Principle Voting Delegate to DICOM, College of American Pathologists
1998-2000	Member, SNOMED Editorial Board, College of American Pathologists
1999-2002	Chair, Informatics Committee,College of American Pathologists
1999-2001	Member, Council on Practice and Education (COPE),College of American Pathologists
2000-2001	Member, Education Cluster Committee of the Council on Practice and Education (COPE), College of American Pathologists
2000-	National Institutes of Health *Center for Scientific Review* Site Visit Study Section, National Supercomputing Centers Special Opportunity Funding for Pathology Informatics

2001-2003	Advisor, SNOMED Editorial Board
2001-2004	CAP Delegate to DICOM Structured Reporting Working Group
2001-	Laboratory and Diagnostic Anatomic Pathology Image Exchange Standards Task Force - Association of Pathology Informatics
2001-2002	Member, Information Sciences Council, College of American Pathologists
2003-2004	Advisor, Informatics Committee, College of American Pathologists
2002-2004	Training and Education and Education Committee Chair, Association for Pathology Informatics
2005-2006	Vice President, Association for Pathology Informatics
2006-2007	President-Elect, Association for Pathology Informatics

Community Service

2001-	Senior Managing Editor and Chief Information Officer, American Foundation for GreekLanguage and Culture (www.afglc.org)

Patents

6,759,245. CELL CULTURE SYSTEMS AND METHODS FOR ORGAN ASSIST DEVICES. **Toner; Mehmet** (Wellesley, MA); **Tilles; Arno W.** (Cambridge, MA); **Balis; Ulysses J.** (Peabody, MA); **Yarmush; Martin L.** (Newton, MA); **Cosman; Maury D.** (Woburn, MA); **Dimilla; Paul A.** (Dover, MA)

6,562,616 Methods and devices for cell culturing and organ assist systems. **Toner; Mehmet** (Wellesley, MA); **Yarmush; Martin L.** (Newton, MA); **Balis; Ulysses J.** (Peabody, MA); **Tilles; Arno W.** (Cambridge, MA)

Technology Transfer

Automated Barcode tracking system for Anatomic Pathology Workflow. Licensed to Impac Medical Systems by MGH Corporate Sponsored Licensing and Research, 2005. Royalty terms: $250,000.

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9. Balis UJ Imaging input technology. Clin Lab Med. 1997;17:151-174.

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2. Balis UJ, editor. Imaging in the Clinical Laboratory. In: Pathology Clinics of North America. Philadelphia: W.B. Saunders; 1997.

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Scientific Advisory Boards,

1. Aperio Technology, Vista. CA
   http://www.aperio.com/company/Aperio-bd-of-directors.asp
2. Impac Medical Systems, San Jose, CA
   http://www.impac.com/company/pressroom/ind_prs/lpr58050503.html
3. Living Microsystems, Inc., Watertown MA
   http://www.livingmicrosystems.com/ourTeam.html
4. Cellpoint Diagnostics, Inc. Watertown MA

Clinical Communications

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2. Skjei, E. Bringing order to data chaos. *(Telephone interview contents quoted within article). CAP Today* November 2003.

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2. Flotte TJ, Saleemuddin A, Balis U, Wide-field digital microscopy produces diagnostic quality images for telepathology. Modern Pathol 2003;16(1): 1469.

EXHIBIT K

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April 13, 2007

Douglas E. Ringel, Esq.
KENYON & KENYON LLP
1500 K Street, N.W.
Washington, D.C. 20005

Re: Scope of Discovery and Supplementation of Responses to Discovery Served in *Vision II* (Civil Action No. 05-CV-10614-GAO)

Dear Doug:

This letter in part responds to your letter of April 12 regarding the proper scope of discovery in this matter. We appreciate Vision's agreement to produce for inspection the requested code for the Bond systems and we will work with you and your client to coordinate the scheduling of this inspection – presumably in the latter half of May.

Ventana will definitely move for a permanent injunction immediately upon prevailing in the liability phase. Ventana initially moved for a preliminary injunction, only withdrawing that motion based on an expedited trial date on the merits. Given the irreparable injury Ventana has suffered and will continue to suffer due to Vision's infringement and the delay caused by the BioGenex Appeal and related stay in this matter, Ventana will not agree to a further delay during a further discovery period and trial on damages and willfulness. Given the *eBay* decision, we agree that fact discovery should be extended to the propriety of the issuance of a permanent injunction in this matter, including discovery relevant to the *eBay* factors. During the last fact discovery period the parties used their allotted interrogatories, albeit on many interrogatories that were related to Ventana's motion for preliminary injunction and thus, per agreement, never substantively answered. Would Vision agree to allow each party to serve a limited number of additional interrogatories on this issue? If so, we believe any such agreement should be documented in the scheduling-related stipulation.

Regarding supplementation of the fact discovery identified in your letter, Ventana agrees to provide supplemental fact discovery responses and production on the narrow issues of licensing and commercial success. However, we do not agree to broader re-opening of fact discovery on validity or re-opening of expert discovery on these issues.

Ventana also hereby requests that Vision promptly supplement its document production and responses to discovery served in *Vision II* (Civil Action No. 05-CV-10614-GAO), specifically by producing documents responsive to requests for Production Nos. 1-27 and Interrogatory Nos. 1-25. As you are aware, the Federal Rules impose an obligation on a party to timely supplement its discovery responses and disclosures whether or not specifically requested by a party. However, we believe at least the following document requests and interrogatories are very likely to require supplementation given the passage of time while this matter was stayed:

INTERROGATORIES:

3. Describe in detail all differences in design between the BOND – OCR and the devices found to infringe the PATENT IN SUIT in the September 30, 2004 Memorandum and Order in VISION I.
7. Identify every person who has participated in or contributed to the conception, research, design, development, engineering, testing, or manufacture of the use of optical character recognition in the BOND SYSTEM, and for each person state the nature and extent of his or her participation or contribution and the time period or periods during which he or she so participated or contributed.
8. Identify every person who has participated in or contributed to the marketing or sale of the BOND - OCR system, and for each person state the nature and extent of his or her participation or contribution and the time period or periods during which he or she so participated or contributed.
9. Identify all changes or revisions to all manuals or specifications RELATING TO the use of optical character recognition in the BOND SYSTEM or the BOND - OCR.
12. Identify in detail any demonstrations, placements, loans, leases, or sales of the BOND – OCR to any customer or potential customer in the United States, including the identity of the customer or potential customer, date, terms or proposed terms including any consideration received by YOU, and any related products.
19. Describe the manner in which the BOND-OCR is installed at customer sites in the United States, including without limitation the identity of the PERSONS and parties responsible for performing installation of the BOND-OCR.
20. Describe the nature of maintenance services provided for the BOND-OCR in the United States, including without limitation the identity of the PERSONS and parties responsible for providing maintenance of the BOND-OCR.
21. If YOU contend that there are any substantial uses of the BOND-OCR that are not described in the User Manual (VBS-OCR 07887-08072), describe any such

uses and IDENTIFY the PERSONS, if any, who use the BOND-OCR in such a manner.

22. If YOU contend that there are any substantial uses of the BOND-OCR that are not described in the Service Manual (VBS-OCR 6981-7566), describe any such uses and IDENTIFY the PERSONS, if any, who use the BOND-OCR in such a manner.

DOCUMENT REQUESTS:

1. All DOCUMENTS RELATING TO engineering or technical specifications, flowcharts, manuals or guides referring to, describing, documenting or relating to the functionality, operation, structure or architecture of the BOND - OCR.
2. All draft, proposed or final specifications for the BOND – OCR.
4. All DOCUMENTS RELATING TO engineering or technical specifications, flowcharts, manuals and guides referring to, describing, documenting or relating to the functionality, operation, structure or architecture of any ID SCANNER used or included in the BOND - OCR.
5. All DOCUMENTS RELATING TO the use of optical character recognition technology to read information on a slide or other device used for mounting or containing biological material.
6. All DOCUMENTS RELATING TO the use of optical character recognition technology in any AUTOMATED BIOLOGICAL STAINING DEVICE OR RELATED PRODUCT, including, without limitation, the BOND – OCR.
7. All DOCUMENTS RELATING TO the use of an ID SCANNER in the BOND – OCR.
8. All DOCUMENTS RELATING TO the manufacture, functionality and specifications of any ID SCANNER used in the BOND – OCR.
9. All DOCUMENTS RELATING TO any alternatives to bar codes or bar code scanners, in any AUTOMATED BIOLOGICAL STAINING DEVICE OR RELATED PRODUCT.
10. All DOCUMENTS RELATING TO any similarities, differences or comparisons between the uses of or reading of bar codes, and the use of optical character recognition.
11. All DOCUMENTS RELATING TO the issue or question of whether the use of optical character recognition in any AUTOMATED BIOLOGICAL STAINING DEVICE OR RELATED PRODUCT, infringes or would infringe or would be judged to infringe the patent in suit, whether literally or under the doctrine of equivalents.
12. All DOCUMENTS RELATING TO any sales projected or anticipated sales or offers to sell the BOND – OCR.
13. All minutes or records of meetings of your directors, officers and/or employees where the BOND - OCR was discussed, or where optical character recognition was discussed.

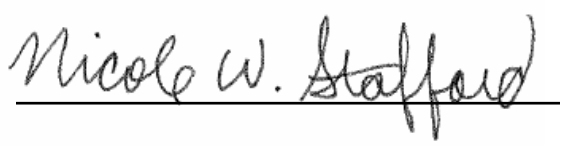
15. All DOCUMENTS distributed to customers or potential customers relating to the BOND – OCR.
16. All DOCUMENTS RELATING TO marketing of the BOND – OCR.
17. All DOCUMENTS RELATING TO competitive information, market share, and competitive analyses and projections RELATING TO the BOND – OCR and any other AUTOMATED BIOLOGICAL STAINING DEVICE OR RELATED PRODUCT.
18. All DOCUMENTS RELATING TO any advantages resulting from sales or projected sales of the BOND – OCR, including, without limitation, any increased sales, or commitments for sales, of other products, including reagents.
22. ALL DOCUMENTS RELATING TO any demonstrations, placements, loans, leases, or sales of the BOND – OCR to any customer or potential customer in the United States.
25. All DOCUMENTS RELATING TO any activity by YOU, including through YOUR sales and/or marketing staff, to address the impact on YOUR customers of a change from slide barcodes to OCR labels.
26. All DOCUMENTS RELATING TO a negative response by YOUR customers to the use of OCR technology in YOUR AUTOMATED BIOLOGICAL STAINING DEVICE OR RELATED PRODUCT.
27. All DOCUMENTS RELATING TO calibration or pre-programming of scanner technology in YOUR AUTOMATED BIOLOGICAL STAINING DEVICE OR RELATED PRODUCT.

Moreover, Vision's supplemental response to Interrogatory 3 should describe all differences in design, if any, between the current BOND – OCR and BOND – OCR that was the subject of an inspection and Rule 30(b)(6) deposition in 2005, including those changes referred to in your letter of April 12.

We look forward to receiving Vision's supplemental responses and production.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation



Nicole W. Stafford

EXHIBIT

L

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May 3, 2007

VIA E-MAIL

Nicole W. Stafford, Esq.
Wilson Sonsini Goodrich & Rosati
8911 Capital of Texas Hwy. North
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Re: Vision BioSystems (USA) Trading, Inc. v. Ventana Medical Systems, Inc., 03-CV- 10391 GAO (D. Mass.); Ventana Medical Systems, Inc. v. Vision BioSystems, Inc., 05-CV-10614 GAO (D. Mass.) Our Ref.: 13497/1

Dear Nicole:

This letter follows up on our conversations of April 30 and May 1 and also responds to your letter of May 1.

In our conversation of April 30, I expressed our view that the *KSR* decision warranted supplemental expert reports on obviousness. In our conversation of May 1, you indicated that Ventana would agree to having Vision provide a report from its engineering expert, but Ventana objected to Vision providing a report from its pathologist expert. Your letter of May 1 repeats this. It appear that both parties agree that supplementation is needed in view of *KSR*. We just disagree on what supplementation is appropriate.

In *KSR*, the Supreme Court ruled that the obviousness inquiry must not be confined "by overemphasizing the importance of published articles and the explicit content of issued patents," but instead must consider "market demand" and whether a person of ordinary skill "facing the wide range of needs created by developments in the field of endeavor" would have seen the benefit of combining elements known in the art. *KSR* Slip. Op., p. 20. This "market demand" or "need" consideration is repeatedly emphasized in the decision. *Id.*, p. 13 ("When a work is available in one field of endeavor, design incentives and other *market forces* can prompt

variations of it, either in the same field or a different one."), p. 14 ("Often it will be necessary for a court to look to … the effects of *demands* known to the design community or present in the *marketplace*"), p. 15 ("it often may be the case that *market* demand, rather than scientific literature, may often drive design trends."), p. 17 ("When there is a design *need* or *market pressure* to solve a problem, … a person of ordinary skill has good reason to pursue the known options within his or her technical grasp.")

The new "market" inquiry set forth in *KSR* requires consideration of the needs of the customers created by developments in the field, consideration of whether there were known solutions for meeting those customer needs, and consideration of whether a person of skill in the art would have seen the benefits of combining elements known in the art to meet those customer needs. In this case, the customers are pathologists. Accordingly, to present this "market" inquiry evidence under *KSR*, it is appropriate that we present expert testimony regarding the needs of customers from the perspective of a customer, i.e., a pathologist, Dr. Balis.

Ventana's position that expert supplementation under *KSR* should be limited to supplementation only from experts who previously submitted reports on obviousness is a transparent attempt to allow Ventana to submit "market" inquiry evidence from its pathologist, Dr. Hicks, while preventing Vision from presenting similar evidence from its own pathologist, Dr. Balis. We obviously cannot agree to allow Ventana to present expert pathologist testimony under *KSR* if Ventana cannot agree that Vision is entitled to the same opportunity.

To be clear on our proposal, taking into account *KSR*, we request Ventana's agreement to Vision serving a report from Dr. Balis, as follows:

Dr. Balis will submit an expert that addresses the "market" inquiry under *KSR*, specifically addressing the needs of the customers created by developments in the field, consideration of whether there were known solutions for meeting those customer needs, and consideration of whether a person of skill in the art would have seen the benefits of combining elements known in the art to meet those customer needs.

Because this inquiry addresses the ultimate issue of obviousness under the new standard, because addressing the ultimate issue of obviousness requires consideration of secondary indicia (where raised), and because of the supplemental fact discovery relating to commercial success, our proposal is that Dr. Balis would address secondary indicia (as raised by Dr. Hicks).

Dr. Balis would address the inquiry under *KSR* based on the prior art already addressed, with the exception that Dr. Balis will also address U.S. Patent No. 5,122,432 to McCulloch. There is no prejudice to Ventana in Vision's including the McCulloch reference, as Ventana and its experts have already addressed the McCulloch reference in the *Biogenex* case.

In the penultimate paragraph of your May 1 letter you refer to a letter from Elizabeth Leff dated September 12, 2005. That letter reflected the parties' negotiations two months prior to a scheduled November 2005 in view of the facts and circumstances at the time and in view of the discovery that then-needed to take place in the relatively short time left to the scheduled

November 2005 trial date. The circumstances since then, however, have changed, and it is unreasonable to assume that the referenced correspondence was meant to freeze the obviousness record even if circumstances changed substantially, which they have. The law of obviousness has changed dramatically, and facts highly pertinent to commercial success have transpired over the last two years. In fact, your own letter reflects these changed circumstances, as Ventana itself proposes to supplement the obviousness record in view of *KSR*.

I understand from our conversation May 1 and your letter of May 1 that Ventana objects to allowing Vision to serve any report from Dr. Balis addressing any issue relating to obviousness. If Ventana is willing to reconsider its position in view of the above, please let me know.

Sincerely,

Douglas E. Ringel

658511

EXHIBIT M

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May 1, 2007

Douglas E. Ringel, Esq.
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Re: Civil Action No. 05-CV-10614-GAO

Dear Doug:

This letter is in furtherance of our call today and in response to your letter of yesterday. During today's call, I presented the following proposal as a compromise in an attempt to amicably resolve the present dispute regarding the status of expert validity discovery in *Vision I*:

- Both parties can supplement their current expert reports on patent validity in *Vision I* to take into account any changes in the law set forth in the *KSR* decision.[1] Timing of supplementation would be at the same time as the dates we discussed for initial and responsive reports on infringement of the Bond-OCR before this issue arose.

- To the extent a party believes that a particular addition or modification of an expert report on validity is not an appropriate supplementation based on the *KSR* (or other)[2] decision, the party need not raise that issue now, but can raise this issue with the Court any time after receiving the objected-to supplemental validity expert report. Moreover, nothing in this proposal should be deemed as an admission by Ventana that any of the ways in which Vision identified it intended to supplement its validity expert reports in your April 16 letter are appropriate supplementation based on *KSR* (or other)[3] decision.

- There will be no new experts or witnesses on patent validity not already identified and allowed in *Vision I*.

[1] Although not discussed during our call, we would be willing to similarly allow for supplementation of existing expert validity reports based on changes in the law in the Federal Circuit decisions referenced in your April 16 letter to the extent any such changes remain in light of the *KSR* decision.
[2] *See* note 1.
[3] *See* note 1.

- We can probably agree to tentative dates we had previously discussed. In our call, we did discuss that we may need some additional time for fact discovery in light of Vision's 50-60,000 pages of supplemental production and the necessary code inspection and that we may also need more time for expert depositions given our conflict in July. However, we currently believe that we can work within the previously discussed deadlines.

- Ventana firmly believes that it is entitled to seek a permanent injunction at the liability phase of the trial. However, as a compromise to Vision, Ventana will forego seeking a permanent injunction until the remedy phase of the case if Vision agrees to Ventanas's proposal. To the extent, an agreement is not reached, Ventana may seek a permanent injunction immediately upon the successful conclusion of the liability phase of this trial.

- To the extent an agreement is not reached and Vision insists on new validity experts or witnesses or other wholesale re-opening of expert validity discovery not tied to changes in law by *KSR* or other decision or changes in facts:

    - We will oppose and will seek expenses and fees from previous rounds of expert discovery. Ventana has already been subjected to two rounds of expert reports and depositions on validity at great expense due to Vision's prior belated request to re-open expert validity discovery.

    - Ventana does not agree to the tentative dates previously discussed if expert validity is re-opened as suggested by Vision. These dates were discussed in the context of the parties' understanding that validity expert discovery was closed. It was only after the parties tentatively identified dates that Vision first stated its intention to seek to re-open expert validity discovery. Moreoever, Ventana believes these dates are unworkable with the re-opening of validity discovery suggested by Vision.

During our call you stated that Ventana's proposal was unacceptable to Vision and that you expected to file a motion for leave to file the supplemental validity expert reports outlined in your April 16 letter to raise this issue with the Court. Our proposal remains and we respectfully request Vision to reconsider its position in light of the prior agreements and statements of the parties.

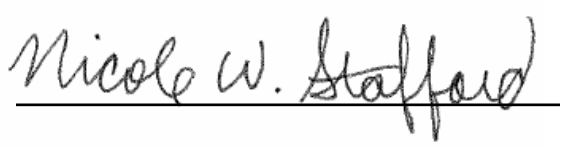
As indicated on numerous occasions, Ventana is not amenable to Vision providing supplemental validity expert reports as outlined in your April 16, 2007 letter. The proposal in your April 16 letter would amount to wholesale re-opening of validity expert discovery and is

contrary to numerous agreements and statements of the parties. As only one example, Vision previously agreed that it would not call any witnesses to testify on patent validity that had not been previously identified in Vision I and that supplementation of commercial success documents by Ventana would not be a basis for re-opening validity discovery. Your April 16 letter, and in particular your current attempt to have Dr. Balis testify on matters of patent validity, is in direct conflict with this agreement. I forwarded correspondence documenting this agreement to you on April 23, but have received no written response as to whether or not Vision will honor its agreement. Moreover, as we discussed during in this and other calls, none of the specific ways in which Vision intends to supplement its validity expert reports as reflected in your April 16 letter are based on the Supreme Court decision in the *KSR* case or any new, or changes in the, facts or law.

Please contact me with any questions or to further discuss this matter. I look forward to amicably resolving this dispute without involving the Court.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation



Nicole W. Stafford

EXHIBIT N

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SUPREME COURT PRACTICE

Monday, April 30, 2007

Some thoughts about *KSR v. Teleflex*: The "Marketplace" Test for Obviousness

Posted by Gretchen Sund at 01:35 PM

The following commentary is from Michael Barclay of Wilson Sonsini Goodrich & Rosati. The views expressed in this posting are those of the individual author, and do not necessarily reflect the views of his law firm or any of his clients.

This decision makes it far easier to invalidate patents based on obviousness. Thus, this is the most important patent case of the last 20 years, and perhaps since the passage of the 1952 Patent Act. Virtually every litigated patent case includes an assertion of obviousness – and ones that might not have included that defense up until now are more likely to do so. The PTO examines every patent application for obviousness. *KSR v. Teleflex* will thus have an enormous impact on both the prosecution and litigation aspects of patent practice.

The Supreme Court continues to take a close look at the Federal Circuit's jurisprudence and how the Court of Appeals for the Federal Circuit (CAFC) interprets the Patent Act or other relevant statutes. In *eBay v. MercExchange*, decided in May 2006, the Court unanimously reversed the CAFC's reading of 35 U.S.C. Section 283, where the CAFC had engrafted a "general rule" requiring permanent injunctions in favor of a victorious patent owner, even though the language of the statute said no such thing. In *Medimmune v. Genentech*, decided in January 2007, by an 8-1 vote, the Court reversed the CAFC's reading of Article III's case or controversy requirement, and of the declaratory judgment statute. In *Microsoft v. AT&T*, decided the same day as *KSR v. Teleflex*, the Court reversed the Federal Circuit's reading of 35 U.S.C. Section 271(f) by a 7-1 vote.

Now in *KSR v. Teleflex*, the Court has again reversed the CAFC's reading of a statute, namely 35 U.S.C. Section 103. At the outset, the Court's unanimous opinion abolished the CAFC's imposition of a "teaching, suggestion, motivation" (TSM) test for obviousness. Slip Opn. at 11. By way of background, there are two ways to invalidate a patent based on prior art: (1) Anticipation under 35 U.S.C. Section 102, which requires a showing that the identical thing was invented earlier in a single piece of prior art; or (2) obviousness under 35 U.S.C. Section 103:

A patent may not be obtained though the invention is not [anticipated], if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

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Before the creation of the Federal Circuit in 1982, Supreme Court cases interpreted Section 103 without adopting the TSM test. For example, *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966), stated:

Under 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized . . . . As indicia of obviousness or nonobviousness, these inquiries may have relevancy.

The CAFC adopted the TSM test even though the language of Section 103 lacked any such requirement. Adding the TSM test to the statutory and *Graham v. John Deere* requirements made it more difficult to invalidate patents as obvious, since either an express or implied "teaching, suggestion, motivation" had to be shown. The CAFC's main rationale for the TSM test was to avoid invalidating patents as obvious based on a hindsight analysis, and most patent practitioners liked the TSM test both for this reason and because it usually seemed straightforward to apply.

Having abolished the TSM test, the Court had to figure out what to replace TSM with. The replacement test can be summarized as a "marketplace" test – Justice Kennedy's well-written opinion uses phrases such as "marketplace," "market forces," "market demand" and "market pressure" no less than five times in describing replacement formulations and in holding claim 4 of the Teleflex patent obvious as a matter of law. Slip Opn. at 13, 14, 15, 17, 20.

a. For example, in summarizing the Supreme Court's prior decisions on obviousness, the opinion states (Slip Opn. at 13):

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. Sakraida and Anderson's-Black Rock are illustrative – a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

b. Immediately thereafter, the opinion elaborates as follows (Slip Opn. at 14; citation omitted):

> Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit. As our precedents make clear, however, the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.

c. Next, the Court rejected the CAFC's sporadic requirement of a "teaching, suggestion,

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motivation" that appears in published literature or patents, and again discussed the "market demand" approach to determining if something is obvious (Slip Opn. at 15):

> The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents. The diversity of inventive pursuits and of modern technology counsels against limiting the analysis in this way. In many fields it may be that there is little discussion of obvious techniques or combinations, and it often may be the case that market demand, rather than scientific literature, will drive design trends. Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility.

d. Finally, after noting that "any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed," Slip Opn. at 16, the Court overruled the CAFC's prohibition against proving obviousness by showing that the combination of elements was "obvious to try" – again, a significant erosion of the CAFC's jurisprudence. The Court stated (Slip Opn. at 17; citation omitted):

> The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103.

The Court applied its reasoning to conclude that claim 4 of the Teleflex patent was obvious as a matter of law. It noted that there "existed a marketplace that created a strong incentive to convert mechanical pedals to electronic pedals, and the prior art taught a number of methods for achieving this advance." Slip Opn. at 20. In so doing, the Court did not merely vacate the CAFC's decision; it reversed the CAFC and ordered reinstatement of the district court's summary judgment of obviousness. The Court noted that the "conclusory" affidavits of Teleflex's experts were no bar to summary judgment on the record of this case. Slip Opn. at 23.

Abolishing the TSM test, then, will make it easier to invalidate patents, which is why *KSR v. Teleflex* is of such importance. As an example, many patent practitioners working in computer or electronics technologies have seen the following type of patent in the last 10 years. Many people filed for patents in the early to mid-1990's that claimed little or nothing more than (a) a well known, prior art process or technology – such as methods for commercial sales, computer networking, security, or the like – that (b) were performed over the Internet, which the patent applicant assuredly did not invent either. The patent would not be anticipated, because the well known process had not been previously performed over the Internet before it became popular in the mid-1990's. The patent owner would also argue that the patent was not obvious, since there was no "teaching, suggestion, or motivation" to combine the prior art process with the prior art Internet, again because the Internet was new. While the parties could debate the latter point – an "implied" TSM would seem likely in many cases – this has led to much litigation and licensing demands over the last decade. Under *KSR's* "marketplace" test, the market demands of going to the Internet could be evidence of obviousness.

The Supreme Court appears to be concerned with some public pronouncements about patent quality and the number of dubious patents. For example, the rate of issuance of new patents has increased significantly since the CAFC's TSM rule, far beyond what can be attributed to mere population growth. When U.S. Patent No. 7,000,000 issued in February 2006, the USPTO issued a press release about the event. That press release noted that "It took 75 years to get from patent No.1 to patent 1 million. It has taken less than one tenth of that time [i.e. only 6 years] to go from 6 million to 7 million patents."
While quantity might not be an indication of lack of quality, the acceleration of the issuance of patents is of some concern.

The level of skill is likely to become very important in future obviousness determinations. Since TSM has been abolished as a doctrine, the level of ordinary skill remains as a factor under the statute and under *Graham v. John Deere*. If the level of skill is high, many more things will be obvious – a genius will find lots of inventions obvious. If the level of skill is very low, an invention is less likely to be obvious. While the level of skill was not frequently the subject of much debate in patent suits – its importance paled by comparison to the question of whether a TSM existed – level of skill may well be more of a key factor going forward. *See, e.g.*, Slip Opn. at 16-17.

There is an interesting interplay between an enabling disclosure under Section 112 of the Patent Act and obviousness. Among other things, section 112 requires that the patent specification "contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same." Note that the level of skill is relevant to whether the patent is enabling. If the level of skill is low, more detail must be included in the patent disclosure to make it enabling; less detail is required if the level of skill is high. However, as discussed in the previous point, if the level of skill is high, the patent is more likely obvious.

For patents with a skimpy disclosure, an accused infringer may wish to put the patent owner to the dilemma of facing (a) an enablement defense if the level of skill is low, so the skimpy disclosure isn't sufficiently enabling; or (b) an obviousness defense if the level of skill is high enough to avoid the enablement defense. Patent prosecutors going forward can make litigation counsel's life easier by putting a meaningful amount of background and detail in the patent application, giving the litigators the flexibility of arguing for an enabling disclosure to someone of a low level of skill, and for a finding of non-obviousness because of that same low level of skill.

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EXHIBIT O

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April 30, 2007

VIA FEDERAL EXPRESS

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Re: *Vision II* (Civil Action No. 05-CV-10614-GAO)

Dear Mr. Ringel:

Enclosed please find documents bates numbered VEN 1036693 – VEN 1037227, some of which are designated "Confidential Pursuant to Protective Order".

Please direct your questions to Nicole Stafford.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

Pat Skinner
Paralegal

Encl.
cc: Robert J. Muldoon, Jr. (w/o encl.)

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EXHIBIT P

US005122342A

United States Patent [19]

McCulloch et al.

[11] Patent Number: 5,122,342

[45] Date of Patent: Jun. 16, 1992

[54] **BIO-FLUID ASSAY APPARATUS**

[75] Inventors: **Peter F. McCulloch**, Wilmslow; **Robert J. F. Moore**, Stockport, both of England

[73] Assignee: **Quatro Biosystems Limited**, Manchester, England

[21] Appl. No.: **378,968**

[22] Filed: **Jul. 12, 1989**

[30] **Foreign Application Priority Data**

Jul. 16, 1988 [GB] United Kingdom 8816982.6

[51] **Int. Cl.**[5] **G01N 35/04**

[52] **U.S. Cl.** **422/65**; 422/67; 364/497; 436/47; 436/48; 436/808

[58] **Field of Search** 422/65, 67, 63; 364/497; 436/47, 48, 808

[56] **References Cited**

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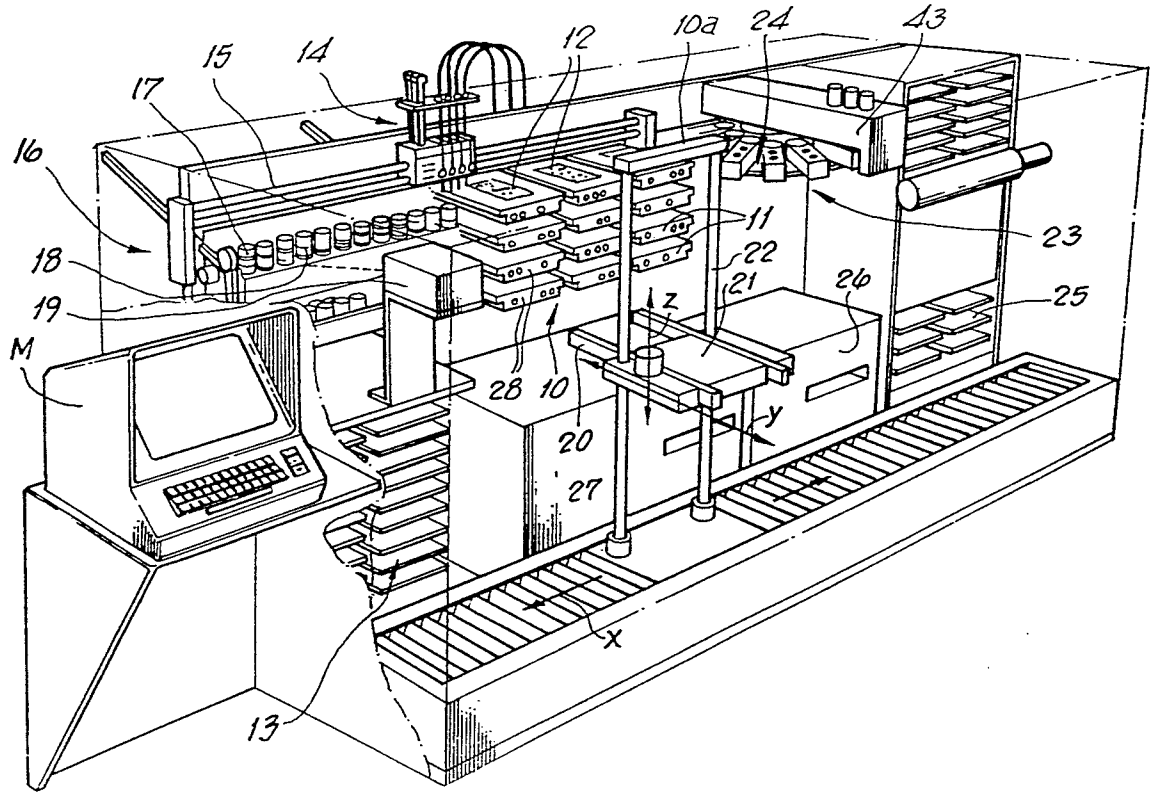
Primary Examiner—Lynn Kummert

Attorney, Agent, or Firm—Watts, Hoffmann, Fisher & Heinke

[57] **ABSTRACT**

There is disclosed micro-processor controlled bio-fluid assay apparatus wherein microtitre plates are on carriers having machine readable labels and wherein the samples of bio-fluid and reagent dispensers also preferably carry machine readable labels whereby the microprocessors which controls movement of the plates through the apparatus can verify correct operation thereof. Movement of the plates is effected by a plate carrier transfer mechanism which has the ability to move the plate carriers in any order and in either direction along each of the x,y and z axes.

12 Claims, 2 Drawing Sheets



U.S. Patent June 16, 1992 Sheet 1 of 2 5,122,342

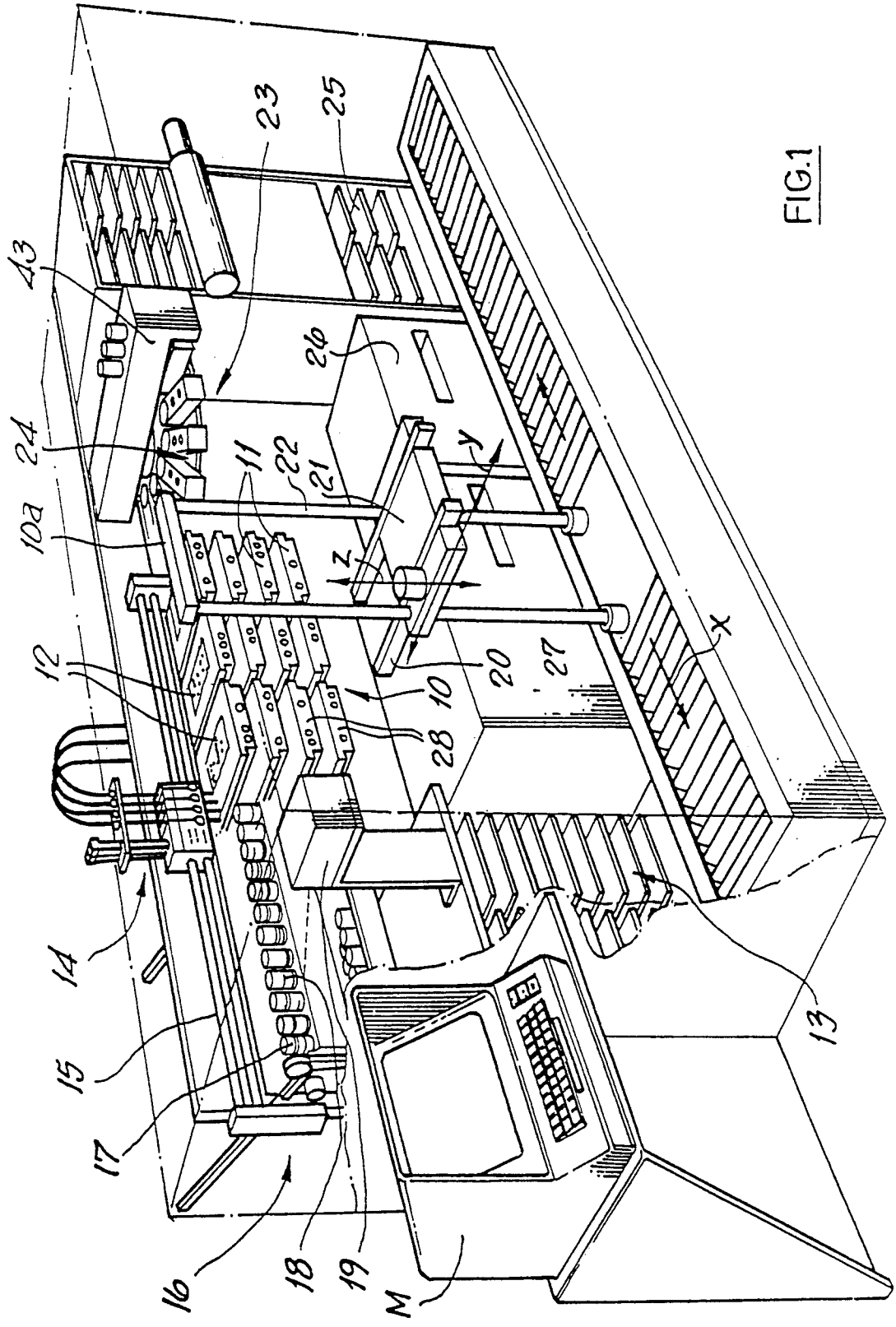


FIG.1

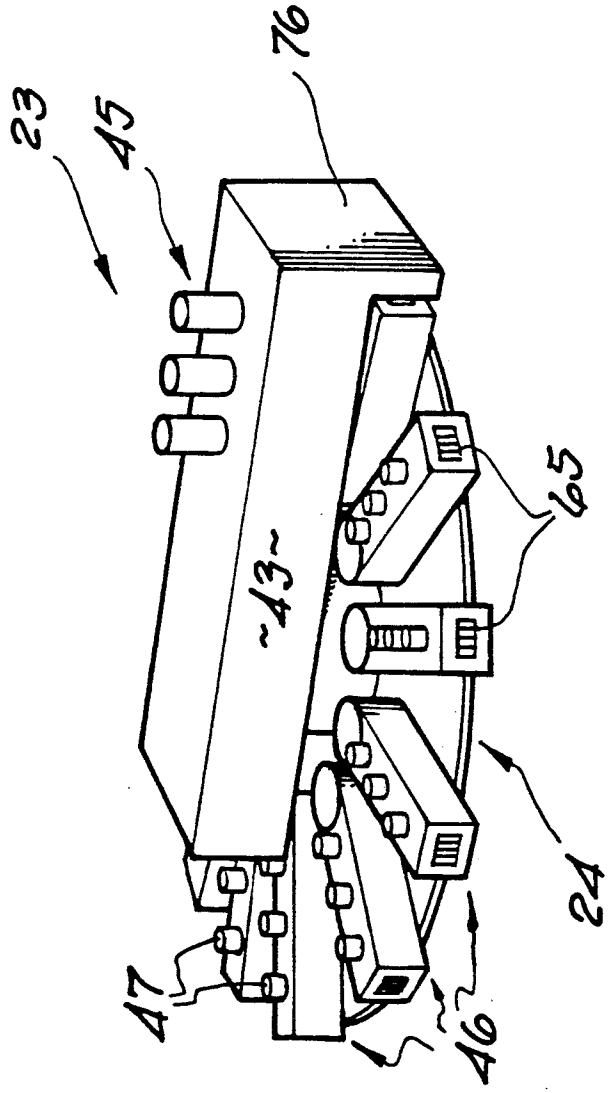


FIG. 2

BIO-FLUID ASSAY APPARATUS

This invention relates to bio-fluid assay apparatus of the kind (hereinafter termed of the kind referred to) wherein measured samples of bio-fluid, for example serum, are introduced into the wells of a microtitre plate (hereinafter 'plate') for subsequent chemical reaction and analysis.

A principal use of apparatus of the kind referred to is the carrying out of immuno-assay tests of serum, the wells of the plates being dosed with antibodies appropriate to the tests to be performed, suitable chemical reagents then being added prior to incubation washing and reading.

It is an object of the present invention to automate the operation of apparatus of the kind referred whilst ensuring a high level of security against error.

According to the present invention there is provided a bio-fluid assay apparatus of the kind wherein measured samples of bio-fluid, for example serum, are introduced into the wells of a microtitre plate for subsequent chemical reaction and analysis, comprising:

a micro-processor controller which may be input with details of patients and the tests required;

a plurality of discrete plate carriers;

an input magazine for said carriers;

an output magazine for said carriers;

a number of operational stations intermediate said input magazine and said output magazine;

plate carrier transport means which is controlled by the micro-processor for collecting plate carriers from the input magazine and progressing them through the successive operational stations and delivering them to the output magazine;

each plate carrier having a uniquely indentifying machine readable label which by reference to the data held by the micro-processor will indicate the particular type of the assay to be effected on the samples carried by the plate; and the transport means including means for reading said labels whereby the micro-processor control means can verify that each carrier taken from the input magazine was loaded and is selected correctly and can confirm the validity of other movements during the assay cycle.

A first operational station may be a transfer station at which the plates receive measured samples of bio-fluid transferred from a sample receiving section by an automatic pipette arrangement.

The sample receiving section may include a reader for machine readable labels on sample tubes to confirm that such are correctly loaded into the sample receiving section.

Other operational stations may include a station where chemical reagents are added to the plates by a reagent dispensing arrangement, a multiplate incubator, a plate washer and a plate reader. The incubator may be of the shaking kind.

The reagent dispensing arrangement may comprise an indexable dispensing head.

The head may comprise a plurality of reagent dispensers, which may be automatic pipettes, any one of which may be indexed to a dispensing position.

The pipettes may have multiple reagent exits.

The dispensing arrangement may further comprise a machine readable label associated with each reagent dispenser and indicating the identity of the reagents

carried thereby and a label reader at the dispensing position.

The reagent dispensers may be operated by a simple set of powered piston plungers at the dispensing position.

The invention will be further apparent from the following description with reference to the figures of the accompanying drawings, which show, by way of example only, one form of bio-fluid assay apparatus embodying same.

Of the drawings

FIG. **1** shows a perspective diagrammatic view of the bio-fluid assay apparatus according to the invention; and

FIG. **2** shows a detail of the reagent dispensing station of the apparatus of FIG. **1**.

The apparatus is controlled by a suitably programmed micro-processor M, which is input with details of patients and the tests required for example Thyroid, Fertility, Steroid, HIV, Hepatitis and so on. Each test may require a plurality of separate assays. An operator will be directed by the micro-processor to load the apparatus with appropriate plates and samples of the patients' bio-fluids on specified carriers at specified locations. Thereafter the transfer of bio-fluid to the plates and progress of the plates through the various operational stations is under the control of the micro-processor which will give a print-out of all completed test results. In general the micro-processor will determine the order in which different assays will be performed to optimize throughput having regard to different residence time requirements at different operational stations for the different assays and other factors.

Turning now to FIG. **1**, it will be seen that the apparatus has an input magazine generally indicated at **10** for plate carriers **11** each loaded with a microtitre plate **12**, and an output magazine **13** which receives the carriers **11** after they have passed through the various operational stations of the apparatus.

The uppermost tier **10***a* of the input magazine **10** defines a transfer station at which the wells of the plates are dosed with measured volumes of bio-fluid transferred thereto by a multi-head automatic pipette arrangement generally indicated at **14** and indexable along the x-axis on rails **15** between the transfer station and a sample receiving section **16** loaded with tubes **17** of sample. The arrangement **14** is also indexable along the y-axis so that the pipette tips can register with any desired wells in a plate located on a carrier at the transfer station. The pipette tips are themselves movable along the z-axis as is obviously necessary for collection and delivery of sample. The pipette tips may be automatically exchanged or washed after each use in known manner. The tubes **17** carry bar-coded labels **18** (preferably printed under control of the micro-processor at the time of data input). A laser bar-code reader **19** which reports to the micro-processor M is provided to verify that the operator has positioned the sample tubes **17** in the receiving section at the locations directed.

Essentially the apparatus includes a plate carrier transfer mechanism comprising a fork **20** advanceable and retractable along the y-axis to engage with the underside of or be withdrawn from beneath a selected plate carrier. The fork **20** moves along the y-axis relative to a support **21** movable upwardly and downwardly along the z-axis relative to a support pillar **22** itself movable from side to side along the x-axis.

In accordance with the invention each of the plate carriers **11** carries a uniquely identifying machine readable label **28** which by reference to the data held by the micro-processor M will indicate the particular type of assay which the plate carried thereby is to undergo. The support **21** carries a reader for the labels **28** and this reader reports to the micro-processor on the identity of each carrier **11** which the fork **20** engages.

In this way the micro-processor can verify that the operator has positioned plate carriers **11** loaded with plates as directed and confirm the validity of other movements during the assay cycle.

Movement of the fork **20** along all three axes is under the control of the micro-processor to collect plate carriers from the input magazine **10** and position them in the transfer station and after they have been dosed with sample move them to a station generally indicated at **23** where reagents appropriate for the assays to be effected are dispensed into the wells of the plates from a rotatably indexable dispensing head **24**.

The station **23**, shown in more detail in FIG. **2**, comprises an indexable dispensing head **24** rotatably mounted below a stationary module **43**. The head **24** is indexed by commands from the micro-processor M. The head **24** comprises a plurality of arms **46** radially extending from its centre of rotation, each arm having a machine readable label **65** located on the face of the distal end thereof, said label **65** being indicative of the reagent carried. The label **65** is read by a label reader **76** attached to the module **43**, which reports to the micro-processor M, enabling verification that the correct reagents are dispensed to the correct wells of each plate presented at the station **23**.

Each of the arms **46** comprises a plurality of reagent dispensers in the form of multi-channel pipettes **47**. The pipettes **47** are filled from containers of stock reagents' which may be located in the arms **46**. Preferably three pipettes each possessing four reagent exit channels are located in each of the arms **46**.

The module **43** has a plurality of powered piston plungers **45** located therein and extensible therethrough to engage with the pipettes **47**. The plungers **45** are actuated, as directed by the micro-processor after verification of the labels **65** to operate the pipettes **47**.

Whilst the reagents are being dispensed the plate carriers remain supported by the fork which executes necessary step movements in the x and y directions.

The fork **20** then moves the plate carrier into an incubator **25** and deposits it for the required residence time before collecting it for transfer to a washer **26** and reader **27** in turn. The incubator may have a variable heat control and may include a refrigerated zone, since it may be desired to carry out the colourmetric stage of some assays, for example the peroxidase catalysed cleavage of 3,3',5,5'-Tetramethylbenzidine Dihydrochloride, at temperatures below room temperature.

The plate carriers may remain supported by the fork whilst in the washer and reader and the fork may execute necessary step movements to enable reading of all wells. Alternatively the plate carriers may be deposited in the washer for a required time and also in the reader if of suitable design. After each plate has been read, the fork **20** transfers it to the output magazine **13** wherefrom it may be retrieved by the operator to enable the used plate to be discarded (or re-read for quality control purposes, for example) a new plate mounted and the carrier repositioned in the input magazine as directed.

The plates engage with the plate carriers such that their position thereon is precisely determined. Equally the plate carriers have projections or grooves which are engageable with complementary formations on the fork and the surfaces which support them at the various operational stations.

The labels **28** and **65** are conveniently magnetically coded and readable by an array of magnetically operable reed switches, but other kinds of label such as bar-coded labels are possible.

Apparatus, according to the invention, may be used, in addition to immuno-assay, in for example, an assay for the cell proliferative potential of bio-fluid. Cells may be seeded in the wells of the microtitre plates and cell growth or proliferation, for example, can be monitored spectrophotometrically after suitable cell staining and washing regimes. In this way, the vaso-proliferative potential of diabetic serum, for example, may be assessed.

It will be appreciated that it is not intended to limit the invention to the above example only, many variations, such as might readily occur to one skilled in the art, being possible, without departing from the scope thereof as defined by the appended claims.

We claim

1. A bio-fluid assay apparatus wherein measured samples of bio-fluid in the wells of a microtitre plate are analyzed comprising:

a micro-processor controller which may be input with data including details of patients and different assays required;

a plurality of discrete plate carriers;

a magazine for said plurality of carriers;

a plurality of operation stations including:

a reagent dispersing station for adding chemical reagents to the plates by a reagent dispensing arrangement;

a plate washing station;

a plate reading station;

plate carrier transport means constructed and arranged to move any plate carrier in either direction along each of x, y and z axes and which is controlled by the micro-processor controller for collecting plate carriers from said magazine and advancing the carriers as required through the plurality of operation stations;

each plate carrier having a uniquely identifying machine readable label which by reference to the data held by the micro-processor controller will indicate the particular type of assay to be effected on the samples carried by each plate;

the transport means including means for reading each label whereby the micro-processor controller can verify that each carrier taken from the magazine is loaded and is selected correctly and can confirm the validity of other movements of each carrier during each assay cycle; and

the micro-processor controller being programmed to determine the order in which different assays are performed.

2. Apparatus according to claim **1**, further including a transfer station at which each plate receives measured samples of bio-fluid transferred from a sample receiving section by an automatic pipette arrangement.

3. Apparatus according to claim **2**, further comprising an incubator station.

4. Apparatus according to claim **2**, wherein the sample receiving section includes a reader for machine

readable labels on sample tubes to confirm that such are correctly loaded into the sample receiving section.

5. Apparatus according to claim **4**, further comprising an incubator station.

6. Apparatus according to claim **1**, wherein said reagent dispensing arrangement comprises an indexable dispensing head comprising a plurality of reagent dispensers.

7. Apparatus according to claim **6**, in which the plurality of reagent dispensers are automatic pipettes, any one of which may be indexed to a dispensing position.

8. Apparatus according to claim **6**, in which the dispensing arrangement further comprises machine readable labels indicating the identity of the reagents carried by each reagent dispenser, and a label reader at a dispensing position to verify that correct reagents are dispensed to correct plates.

9. Apparatus according to claim **8**, in which powered piston plungers at the dispensing position operate the plurality of reagent dispensers.

10. Apparatus according to claim **1**, further comprising a multiplate incubator.

11. Apparatus according to claim **1** further comprising a plate washer.

12. Apparatus according to claim **1**, further comprising an incubator station.

* * * * *

EXHIBIT Q

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Re: ***Vision BioSystems (USA) Trading, Inc. v. Ventana Med. Sys., Inc.,***
Case No. 03-CV-10391-GAO (D. Mass.)

Dear Ms. Leff:

Enclosed are documents Bates numbered VEN 1019673 - 1025255. Please contact me if you have any questions.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

Sarah R. Zimmerman

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January 10, 2005

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Washington, D.C. 20005

Re: ***Vision BioSystems (USA) Trading, Inc. v. Ventana Med. Sys., Inc.*,**
Case No. 03-CV-10391-GAO (D. Mass.)

Dear Ms. Leff:

Enclosed please find documents Bates numbered VEN 1014680 – 1019672. Please contact Roger Chin if you have any questions.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

Judy L. Day
Senior Paralegal

Encl.

cc: Roger J. Chin, Esq. (w/o encl.)

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EXHIBIT S

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September 21, 2005

VIA FEDERAL EXPRESS

Elizabeth A. Leff, Esq.
Rothwell, Figg, Ernst & Manbeck P.C.
1425 K Street, N.W.
Suite 800
Washington, D.C. 20005

Re: ***Vision BioSystems (USA) Trading, Inc. v. Ventana Medical Systems, Inc.*,**
Case No. 03-CV-10391-GAO (D. Mass.)

Dear Ms. Leff:

Enclosed please find documents numbered VEN 1031711 – 1036364. Please contact me if you have any questions.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

Sarah R. Zimmerman

SRZ/jr
Encl.

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